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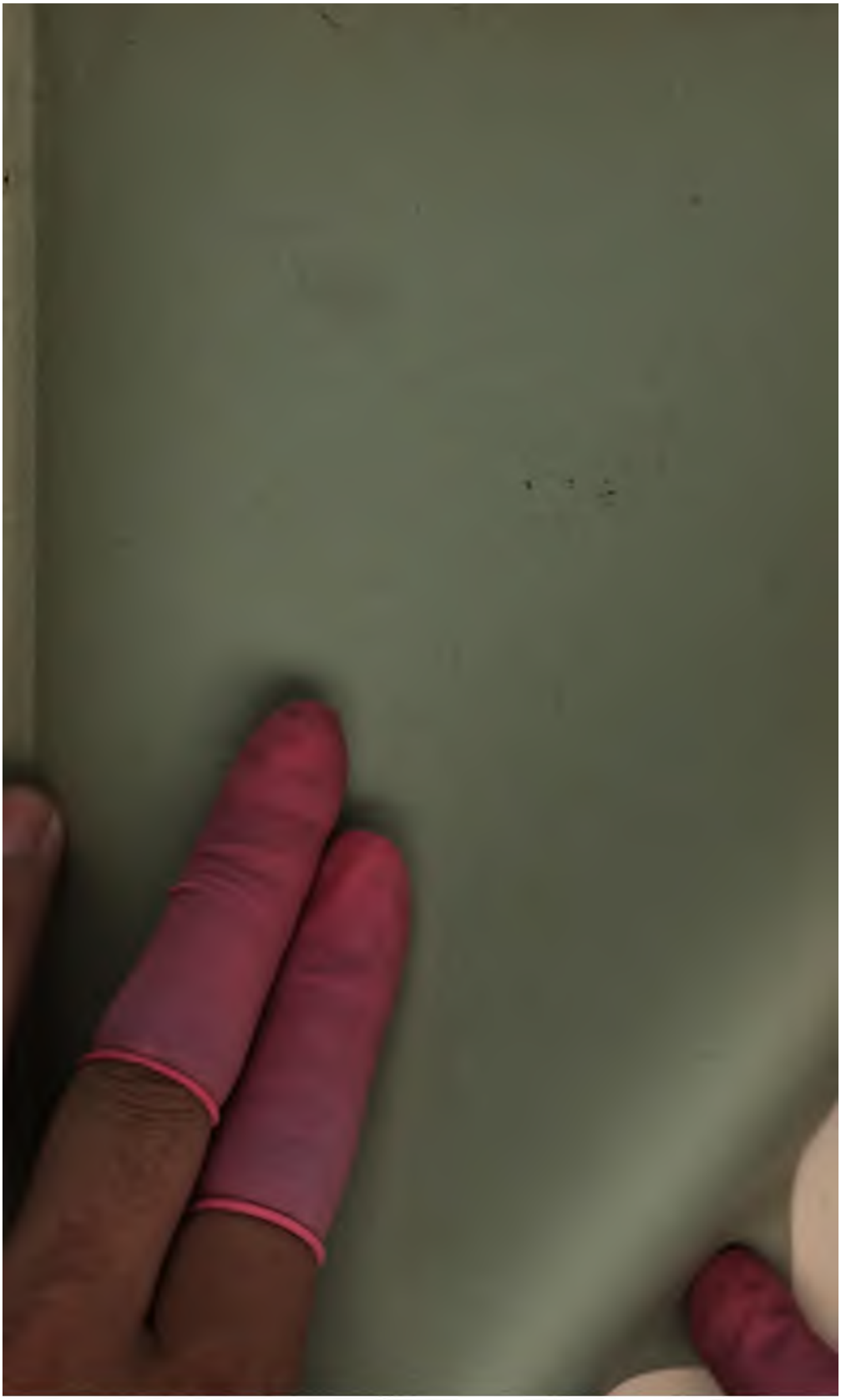

A TREATISE

ON

PHARMACY

FOR

STUDENTS AND PHARMACISTS.

OTTO G. FREYERMUTH.
BY
CHARLES CASPARI, JR., PH.G.,
PROFESSOR OF THE THEORY AND PRACTICE OF PHARMACY IN THE MARYLAND COLLEGE OF PHARMACY.

WITH 288 ILLUSTRATIONS.

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PREFACE.

THE motive for writing this book was, in the main, to supply students of pharmacy with a text-book which, while sufficiently comprehensive to serve as a trustworthy guide, should be devoid of all unnecessary material, such as official and unofficial formulas, etc., readily accessible in the Pharmacopœia and such books of reference as are usually found in drug-stores. The author was repeatedly assured by the late Professor Maisch, and other friends, that such a book was desirable, and, at their request, the task was undertaken. Owing to unavoidable interruptions caused by increased duties, the work, begun in the spring of 1894, was not completed until the autumn of 1895.

Since the present advanced state of professional pharmacy is the fruit of long-continued labors of many competent men in both this country and Europe, no hesitation was had in utilizing their results, the author having, in fact, felt it to be his duty to incorporate with his own experience, extending over twenty-five years of a busy life as a practical pharmacist, the many valuable hints obtainable from numerous well-known writings. Grateful acknowledgment is hereby made for aid derived from such books as *Proceedings of the American Pharmaceutical Association*, *The Art of Dispensing*, Proctor's *Lectures on Practical Pharmacy*, *American Journal of Pharmacy*, Ernst Schmidt's *Lehrbuch der Pharmaceutischen Chemie*, Hager, Fischer u. Hartwich's *Commentar zum Arzneibuch für das Deutsche Reich*, Hager's *Technik der Pharmaceutischen Receptur*, *Die Schule der Pharmacie*, Flückiger's *Pharmaceutische Chemie*, Bornemann's *Die Fetten und Flüchtigen Oele*, and others.

The subjects treated in this book have been grouped under three distinct headings.

Part I. comprises General Pharmacy, which includes the study of weights and measures, specific gravity, the application and control of heat, mechanical subdivision of drugs, and methods of solution and separation, together with a classification and description of the various plant-products and solvents used in pharmacy.

Part II. treats of Practical Pharmacy. This involves a study of the official galenical preparations, together with the many operations of the dispensing-counter. It has been the author's aim to explain as clearly as possible the various processes and apparatus met with in this department, and to point out difficulties likely to be encountered, as well as the remedies therefor. All suggestions made have been tried and verified by the author before offering them, so that statements made are based on actual experience.

Part III. is devoted to Pharmaceutical Chemistry, the study of which is of paramount importance to every pharmacist. While the subject is a very comprehensive one, and undoubtedly entitled to an extensive treatise, it has been confined, in this work, to such compounds as are either officially recognized in the United States Pharmacopœia, or are of special interest to pharmacists.

By a careful analysis of the working formulas of the Pharmacopœia it has been thought possible to render that excellent book more useful to students as well as pharmacists in general. The Pharmacopœia contains a number of valuable tests and assay methods which are unintelligible to the average reader, but which can be made available and interesting by a series of explanations. As such explanations have thus far not been offered in any of the treatises on pharmacy in the English language, the attempt has been made to supply this want.

This book is pre-eminently intended to be one of instruction and an aid in the study and use of the Pharmacopœia. The object constantly in view was to answer, if possible, the many questions of why and wherefore with which students and practising pharmacists

are almost daily confronted. To what extent the writer has been successful in this direction must be left to the judgment of the pharmaceutical profession. He is fully aware that imperfections must of necessity exist in a work covering so extended a field of study, and he hopes that those better able to judge will kindly inform him of any apparent or real defects, so that they may be rectified in a subsequent edition, should such ever be demanded.

The author desires to express his warmest acknowledgments to his friends, A. D. Clark and J. P. Piquett, for valuable suggestions and aid in proof-reading, to all parties who kindly furnished drawings and electros for purposes of illustration, and to the publishers who have spared neither expense nor labor to bring the typography, engravings, and general outfit of the book up to the fullest requirements.

CHARLES CASPARI, JR.

BALTIMORE, September, 1895.

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1 cc = 16.3 mm.
1 g = 15.432 gr.

Rules that should be obeyed.

I. Learn to be neat in all your ways.

II. Never converse when dispensing medicine.

III. Have every thing in its position on the comm

IV. Keep your balance accurate and clean
let nothing defile it; give every-one his proper proportion - no more, no less.

V. Learn to be quick & expert; do your work well
never let haste interfere with accuracy & good work.

VI. Never dispense a ℞ of which you are not absolutely sure; better acknowledge ignorance than that any should suffer.

VII. In case of doubt, consult the prescriber if accessible; otherwise take no risk of life or reputation

VIII. Never substitute.

IX. Always verify your work by calling off & checking with a fellow dispenser; by two witnesses errors are lessened & facts established

X. When handling poisons, always bear in mind the importance of the work you doing; return every article to its proper place at once.

Carelessness causes one-half the mistakes, undue haste the remainder.

PART I.

GENERAL PHARMACY.

CHAPTER I.

PHARMACOPŒIAS.

ALTHOUGH the term *Pharmacopœia* (from the Greek φάρμακον, medicine, and ποιεῖν, to make) is defined by lexicographers as meaning a book of formulas or directions for the preparation of medicines, the word has now received a more liberal construction and is taken to include, besides the foregoing, also descriptions of vegetable as well as mineral and animal drugs, together with appropriate tests for establishing the identity and quality of the same, the whole prepared by some recognized authority.

The necessity for a definite and authoritative standard in the selection and preparation of medicines was long since recognized by all civilized nations, thus the London Pharmacopœia was established in 1618, that of Paris in 1639 and that of Edinburgh in 1699. The first truly national standard was that of France, issued in 1818, which retained the name of its predecessor, the Paris Pharmacopœia, and is even to-day still known as the Codex Medicamentarius. The first United States Pharmacopœia was established in 1820, prior to which time various foreign pharmacopœias had been in use in this country. The British Pharmacopœia, into which were merged the London, Edinburgh and Dublin (established 1807) Pharmacopœias, was first issued in 1864, while Germany did not adopt a national standard until 1872, nearly two years after the restoration of the German empire. Owing to the rapid advances in the science of medicine and pharmacy, frequent revisions have become necessary, and the following table shows the date of the last revised editions of the pharmacopœias of leading nations:

Country.	Date of Issue.	Country.	Date of Issue.
Germany (supplement)	1895	Russia	1891
France (supplement)	1895	Germany	1890
The United States	1893	Great Britain (supplement)	1890
Denmark	1893	Austria	1889
Switzerland	1893	Great Britain	1885
Italy	1892	France	1884
Japan	1891	Spain	1884

The Pharmacopœia of the United States, although without the power of legal enforcement by act of Government, is, nevertheless,

recognized as an authority by the courts, and is the standard employed in the purchase of medical supplies for the Army and Navy of the United States. In some of the States it has been adopted as the legal standard in the enforcement of pharmacy laws, and this plan is likely to be followed by others. The Pharmacopœia as now published represents the joint work of the medical and pharmaceutical professions; but in the early part of this century, when pharmacy had not yet reached the state of a fully developed profession in this country, the apothecary held a rather subordinate position, and therefore had no voice in the compilation of the first national Pharmacopœia, which was adopted in 1820 by a convention of physicians assembled at Washington, D. C., under the presidency of Dr. S. L. Mitchell, the publication of the book being entrusted to a special committee of which Dr. Lyman Spalding was chairman, and both the Latin and English languages being used in the text. In 1830, through some misunderstanding and consequent dissatisfaction, two separate conventions were held for the revision of the Pharmacopœia, one in New York and one in Washington, and at the latter the Government medical service was represented for the first time and participated in the proceedings; at this time provision was also made for regular subsequent revisions every ten years. In the Pharmacopœia of 1840 the Latin version of the text was omitted, and in this revision material aid was also given by the pharmacists, although they had no representation in the convention; numerous improvements in the working formulas appear in this edition. In the convention of 1850 two colleges of pharmacy were duly represented by delegates, and from this time forward the value of pharmaceutical collaboration has been recognized, and its influence is discernible in the many practical details of the Pharmacopœia. Since 1850 the convention for the revision of the Pharmacopœia has assembled in the city of Washington, D. C., regularly in the month of May of every tenth year; all duly incorporated medical and pharmaceutical societies and colleges throughout the United States are entitled to representation by three delegates, the three branches of the Government medical service being also represented by one delegate each. The final revision and publication of the Pharmacopœia, under instructions from the convention, is entrusted to a committee of twenty-five members; this committee in 1880 and again in 1890 was composed of twelve physicians and thirteen pharmacists, under the chairmanship of Charles Rice, Ph.D.

As the Pharmacopœia is in almost daily use by the pharmacist, a short study of its plan and arrangement is desirable for a more intelligent understanding of the text. The titles of all drugs recognized in the Pharmacopœia, whether derived from the vegetable, mineral, or animal kingdom, are conveniently given in three subdivisions known as the *official Latin name*, the *official English name*, and the *official definition*, to which is added an official description, by means of which the identity of all official substances can be

readily established. The following examples will better illustrate the arrangement of pharmacopœial subjects:

ACONITUM	(Official Latin Name.)
ACONITE	(Official English Name.)
The tuber of *Aconitum Napellus*, Linné (nat. ord. *Ranunculaceæ*)	(Official Definition.)
From 10 to 20 Mm. thick at the crown; conically contracted below; from 50 to 75 Mm long, with scars or fragments of radicles; dark brown externally; whitish internally; with a rather thick bark, the central axis about seven-rayed; without odor; taste at first sweetish, soon becoming acrid, and producing a sensation of tingling and numbness, which lasts for some time.	(Official Description.)
CANTHARIS	(Official Latin Name.)
CANTHARIDES	(Official English Name.)
Cantharis vesicatoria, De Geer (class *Insecta;* order *Coleoptera*)	(Official Definition.)
About 25 Mm. long and 6 Mm. broad; flattish-cylindrical, with filiform antennæ, black in the upper part, and with long wing-cases, and ample membranous, transparent, brownish wings; elsewhere of a shining coppery-green color. The powder is grayish-brown, and contains green, shining particles. Odor strong and disagreeable; taste slight, afterwards acrid.	(Official Description.)
PLUMBI CARBONAS	(Official Latin Name.)
LEAD CARBONATE	(Official English Name.)
$2PbCO_3.Pb(OH)_2 = 772.82$	(Official Definition.)
A heavy, white, opaque powder, or a pulverulent mass, without odor or taste. Permanent in the air. Insoluble in water or alcohol, but soluble in acetic or diluted nitric acid with effervescence. When strongly heated, the salt turns yellow without charring, and if heated in contact with charcoal, it is reduced to metallic lead. Its solution in diluted nitric acid yields a black precipitate with hydrogen sulphide, a yellow one with potassium iodide, and a white one with diluted sulphuric acid. One Gm. of the salt strongly ignited in a porcelain crucible, should leave a residue of lead oxide weighing not less than 0 85 Gm.	(Official Description.)

The OFFICIAL LATIN NAME, which very properly is given in the Latin language, owing to its security against change, is intended to be at once simple and distinctive, and must be accepted as representing the drug or preparation more particularly defined in the other subdivisions. In some instances the names by which drugs have been long known have been retained without any special reference to the source, thus *Galla*, *Buchu*, *Cusso*, *Opium*, *Mastiche*, *Senna*, *Kino*, *Kamala*, etc., but in the majority of cases the generic or specific name of the plant or animal yielding the drug has been adopted as the official name, thus *Aconitum*, *Camphora*, *Catechu*,

Ipecacuanha, Coccus, Hyoscyamus, Moschus, Rheum, Senega, etc. In order to avoid confusion a few of the former generic or specific names of plants have been retained as the official names of drugs now known to be derived from a different source, as in the case of *Quassia* from *Picræna excelsa, Cambogia* from *Garcinia Hanburii, Pareira* from *Chondodendron tomentosum,* etc.

As different species of the same genus often furnish different drugs, it becomes necessary in such cases either to employ the full botanical name of the plant to distinguish the official varieties, as *Viburnum opulus* and *Viburnum prunifolium, Rosa centifolia* and *Rosa gallica,* or to select the generic name only for one of the drugs and the full botanical name for others, as in the case of the genus *Rubus,* where the Pharmacopœia has chosen the generic name of the plant, *Rubus villosus,* to designate the root of the blackberry, but the full name of the plant, *Rubus idæus,* as the official name for the fruit of the raspberry.

Whenever different parts of the same plant are officially recognized as distinct drugs, the name of the particular part must be added to the generic or specific name of the plant, thus *Arnicæ Flores* and *Arnicæ Radix, Belladonnæ Folia* and *Belladonnæ Radix,* etc.; to this rule the Pharmacopœia makes an exception in the case of Sassafras bark and pith, both derived from *Sassafras variifolium*—the bark is officially known by the generic name only, while the pith is designated as *Sassafras Medulla.*

In the official names of compound preparations the principal active constituents are as a rule specified, as *Liquor Ferri et Ammonii Acetatis, Tinctura Aloes et Myrrhæ, Trochisci Glycyrrhizæ et Opii, Pilulæ Aloes et Ferri, Mistura Rhei et Sodæ,* but usage has sanctioned a modification of this rule when there are many ingredients, by naming one of them with the addition of an adjective, such as *compositus, a, um* (compound), *aromaticus, a, um* (aromatic), etc., thus making a simple comprehensive title, as *Spiritus Ammoniæ Aromaticus, Tinctura Cinchonæ Composita, Pilulæ Catharticæ Vegetabiles, Pulvis Morphinæ Compositus, Linimentum Sinapis Compositum,* etc.

In the case of chemical compounds where similar combinations of the same elements, or several varieties of the same compound, have received recognition, it is absolutely necessary that the official name include some qualifying term by means of which the character of the substance may at once be recognized, thus *Hydrargyri Chloridum—Corrosivum* and *Mite, Hydrargyri Iodidum—Flavum* and *Rubrum, Ferri Sulphas—Exsiccatus* and *Granulatus,* etc.

The Latin official names are generally used in the singular number, even though the idea of plurality may be essentially connected with the drug, as in the case of Caryophyllus, Galla, Amygdala, Pilocarpus, etc.; this is in accordance with the precedent set by the Roman medical writers. Whenever a part of the plant also appears in the official name the following rule prevails: *Semen* (seed), *Cortex*

(bark), *Radix* (root) are always used in the singular, while *Folia* (leaves) and *Flores* (flowers) are invariably used in the plural.

The OFFICIAL ENGLISH NAME need not necessarily be a literal translation of the official Latin name, in fact it seems very desirable that a drug should have two distinct names officially recognized, the one confined to the official Latin title, admirably adapted to abbreviation and use in prescriptions, while the other may be employed in the ordinary course of conversation and is intended for use in commercial transactions and the daily routine of business, as *Nutmeg* for *Myristica*, *Brandy* for *Spiritus Vini Gallici*, *Black Haw* for *Viburnum Prunifolium*, *Pale Rose* for *Rosa Centifolia*, *Cascara Sagrada* for *Rhamnus Purshiana*, *Pumpkin Seed* for *Pepo*, etc. Occasionally the English name is used in the plural while the Latin name is always used in the singular number, as *Cantharides* for *Cantharis*, *Cloves* for *Caryophyllus*. In the case of chemical compounds the official English name often indicates with greater precision the true composition, as *Solution of Mercuric Nitrate* for *Liquor Hydrargyri Nitratis*, *Ferrous Sulphate* for *Ferri Sulphas*, *Ferric Citrate* for *Ferri Citras*, etc.

In a large number of instances a second English name, which long custom has demanded shall not be ignored, is given as a synonym in the title, although its origin may be unscientific and its retention not in strict accord with the systematic nomenclature of the Pharmacopœia; the synonym invariably follows the official English name and is enclosed in brackets. Among the prominent synonyms found in the Pharmacopœia are *Calomel* for *Mild Mercurous Chloride*, *Epsom Salt* for *Magnesium Sulphate*, *Balm* for *Melissa*, *Labarraque's Solution* for *Solution of Chlorinated Soda*, *Witch-hazel* for *Hamamelis*, *Sweet Flag* for *Calamus*, *Black Draught* for *Compound Infusion of Senna*, *Red Precipitate* for *Red Mercuric Oxide*, *Griffith's Mixture* for *Compound Iron Mixture*, *Tully's Powder* for *Compound Powder of Morphine*, *Citrine Ointment* for *Ointment of Mercuric Nitrate*, *Basilicon Ointment* for *Resin Cerate*, etc.

Several of the official synonyms have been added for the purpose of more clearly expressing the true chemical character of the compounds for which they are used, than is possible with the official Latin or English names, as *Phenylacetamide* for *Acetanilid*, *Sodium Paraphenolsulphonate* for *Sodium Sulphocarbolate*, *Phenyl Salicylate* for *Salol*, *Beta Naphtol* for *Naphtol*, etc.

The OFFICIAL DEFINITION determines the source and character of the drug or chemical as recognized by the Pharmacopœia. In the case of vegetable drugs the botanical name of the plant yielding the drug is composed of two parts, the generic name and the specific name, always written in the same order of sequence; the first or generic name is invariably begun with a capital letter, and is usually employed as the official Latin name of the drug, while the specific name is only begun with a capital letter when derived from a generic name, as in *Cytisus Scoparius*, or from a proper name, as in *Garcinia*

Hanburii, or when it is indeclinable, as in *Aspidosperma Quebracho-blanco*. The necessity for using the full botanical name of the plant to indicate the source of the official drug is clearly shown in the case of the genus *Lobelia*, of which the Pharmacopœia recognizes only the species *inflata*, although two others, *syphilitica* and *cardinalis*, are also well known; of the genus *Grindelia* two species, *robusta* and *squarrosa*, are recognized as furnishing the official drug. Accompanying the botanical name of the plant is the name of the author, printed in Roman type, and following it, enclosed in parentheses, the natural order to which the plant belongs, thus, *Veronica virginica*, Linné (nat. ord. *Scrophulariaceæ*).

In the case of official chemicals it becomes necessary to establish the identity of the compound by expressing its exact composition by means of symbolic formulas; thus in the case of sodium phosphate the formula $Na_2HPO_4+12H_2O$ specifies clearly the kind officially recognized by that name; other varieties of sodium phosphate, such as $Na_2HPO_4+6H_2O$, Na_2HPO_4, or even NaH_2PO_4, or Na_3PO_4 can therefore not be used in prescriptions or official preparations. The official definition of alumen, alum, is $Al_2K_2(SO_4)_4+24H_2O$, showing that the pharmacopœial alum is potassium alum, or, more strictly speaking, potassium and aluminum sulphate; since commercial alum, as a rule, is ammonium alum, the official definition is important, and necessary to establish the chemical character of the compound to be used as alum in prescriptions and official preparations. The Pharmacopœia recognizes as magnesium carbonate a compound for which the symbolic formula $4MgCO_3.Mg(OH)_2+5H_2O$ is given, which shows it to be not true magnesium carbonate, but a substance containing four molecules of magnesium carbonate, one molecule of magnesium hydroxide, and five molecules of water. The official definition for pure morphine, $C_{17}H_{19}NO_3+H_2O$, recognizes a compound containing one molecule (in this case 5.94 per cent.) of water, and for pure quinine $C_{20}H_{24}N_2O_2+3H_2O$, a compound containing three molecules (in this case 14.28 per cent.) of water. Whenever water is expressed in a symbolic formula, as in the five cases above mentioned, it forms an integral part of that formula, and is shown to be an essential constituent of the official compound; in the majority of cases the presence of such water lends to the compound its power to assume the crystalline form, and is then known as water of crystallization, but when not so required it is known as water of hydration, as in the case of the official magnesium carbonate. Every symbolic formula is followed by a number which expresses the molecular weight of the compound, that is, the sum of the weights of the atoms of component elements; thus in the case of the official bismuth citrate, $BiC_6H_5O_7 = 397.44$, the molecular weight 397.44 is equal to the sum of the weights of all the atoms represented in the compound, namely, 1 atom of bismuth $= 208.9$, 6 atoms of carbon $= (11.97 \times 6)$ 71.82, 5 atoms of hydrogen $= (1 \times 5)$ 5, and 7 atoms of oxygen $= (15.96 \times 7)$ 111.72,

or $208.9 + 71.82 + 5 + 111.72 = 397.44$; official sodium carbonate is given as $Na_2CO_3 + 10H_2O = 285.45$, in which case the weight of all the atoms of the crystalline compound, including the water, is accounted for in the molecular weight, 285.45, as follows: 2 atoms of sodium $= 23 \times 2$ or 46, 1 atom of carbon $= 11.97$, 3 atoms of oxygen $= 15.96 \times 3$ or 47.88, ten times 2, or 20 atoms of hydrogen $= 1 \times 20$ or 20, and 10 further atoms of oxygen $= 15.96 \times 10$ or 159.6, or $46 + 11.97 + 47.88 + 20 + 159.6 = 285.45$.

The number following simple elements expresses only the weight of a single atom, as bromine, $Br = 79.76$, sulphur, $S = 31.98$, etc. Atomic and molecular weights are of value in the proper construction of equations for the purpose of demonstrating chemical reactions.

THE OFFICIAL DESCRIPTION. While the official definition is a brief but exact statement of the nature and source of drugs and of the composition of chemicals, the official description amplifies the definition by adding the physical characteristics of drugs, such as shape, size, odor, and taste, together with a statement of possible impurities and adulterations and means for their detection. For chemicals is added a clear account of their physical properties, their behavior toward different solvents, and such tests as shall enable the pharmacist to detect impurities and establish the fulfilment of pharmacopœial requirements. The official description is always printed in small type, and forms a most valuable and important part of the Pharmacopœia.

Dispensatories.

A dispensatory is a commentary on the Pharmacopœia, and, as such, has become indispensable to both physicians and pharmacists. While the text of the Pharmacopœia is confined to the definition and description of drugs and chemicals as well as to the official tests and requirements and accepted formulas for numerous preparations, much valuable additional information is given in the dispensatories, such as historical data, action, and uses, as well as doses of medicines, together with comments on and explanations of pharmaceutical and chemical processes. Besides the official drugs and chemicals, a large number of unofficial remedies and formulas are also treated in detail. Two dispensatories are published in this country: the *United States Dispensatory*, established in 1833, by Wood and Bache, which has now reached its seventeenth edition, and the *National Dispensatory*, established in 1879, by Stillé and Maisch, of which five editions have thus far been published.

CHAPTER II.

WEIGHTS AND MEASURES.

METROLOGY (from the Greek word μέτρον, measure, and λόγος, a discourse) is a study of the art and science of measurements as applied to extension, volume, and weight of matter. Measure of extension may be either of length or of surface, while measure of volume or bulk applies to the cubic contents. Measure of weight is the determination of the gravitating force of bodies, that is, of their attraction by the earth toward its centre, such attraction bearing a direct relation to the quantity of matter contained in a body; hence weight is pressure exerted by a body upon a horizontal plane supporting it. True weight can only be obtained *in vacuo*, where the exact measurements of the force of gravitation cannot be interfered with by atmospheric pressure; all measurements of weight in any medium, such as air or water, must therefore give low results. Ordinary operations of weighing, being conducted in air, give apparent weight of the substance only.

Weighing and measuring being operations of daily occurrence in pharmacy which require care and exactness, a knowledge of the standards of weights and measures in use in this country and elsewhere is absolutely necessary. With more or less modification the standards at present in use in pharmacy in the United States and Great Britain are the same as those formerly employed by the Romans, and which in all probability were by them derived from the more ancient Greek nation. Three different systems of weights are at present employed in all English-speaking nations; namely, avoirdupois weight, apothecaries' weight and metric weight.

AVOIRDUPOIS weight, as its name would seem to indicate, is probably of French origin (*avoir du poids*, to have weight), and was no doubt introduced into Great Britain during the reign of the Norman dynasty; it first appeared in the English statute-books in 1335. Avoirdupois weight is employed in the sale of all commodities except precious metals and precious stones, hence drugs are always bought and sold by pharmacists by this system. In Great Britain avoirdupois weight is also employed in the formulas of the British Pharmacopœia, and is now known there under the name of Imperial weight. In 1824, the value of an avoirdupois pound was defined by law in England to be $\frac{7000}{5760}$ of the old standard troy pound. The divisions of avoirdupois weight are the pound, ounce, drachm, and grain, which are symbolized by the following characters: ℔, oz.,

drm., gr.; each pound contains 16 ounces and each ounce 16 drachms or $437\frac{1}{2}$ grains. The term drachm is rarely employed, quantities less than an ounce being usually designated by common fractions, such as $\frac{1}{16}$ oz., $\frac{1}{8}$ oz., $\frac{1}{4}$ oz., or in grains. The avoirdupois pound containing 7000 grains ($437\frac{1}{2} \times 16$) is the only pound used in the United States and Great Britain except at the mints; the standard pound is the equivalent in weight of 27.7015 cubic inches of distilled water at 62° Fahrenheit and normal barometric pressure.

APOTHECARIES' weight was probably derived from troy weight, which latter was introduced into Great Britain, by merchants from Lombardy, toward the close of the thirteenth century; it is employed altogether in the writing and compounding of physicians' prescriptions, and is divided into grains, scruples, drachms, and ounces, of which 20 grains are equal to 1 scruple, 3 scruples are equal to 1 drachm, and 8 drachms are equal to 1 ounce. The apothecaries' ounce is of the same value as the now obsolete English troy ounce. The following symbols are employed to designate the divisions of apothecaries' weight, and always precede the number indicating the quantity intended, which is expressed in Roman numericals, thus, gr. j, for one grain, ℈ij, for two scruples, ʒiij, for three drachms, ℥iv, for four ounces. As far back as 1266, during the reign of Henry III., a statute was enacted in England which provided that an English silver penny, called a sterling, round and without clipping, should equal in weight 32 wheat-grains, well dried and taken from the centre of the ear, and that of such pence 20 should make 1 ounce, and 12 ounces 1 pound. About 1497, in the time of Henry VII., the weight of the silver penny, however, was changed to the equivalent of 24 wheat-grains. These statutes clearly indicate the origin of the pennyweight and the troy system, from which the apothecaries' weight, still in use at the present day, was subsequently derived. The choice of wheat-grains from *the centre of the ear* arose from a desire for uniformity in size and weight, as did likewise the directions to employ the grain *well dried*. The adoption of troy weight by physicians and pharmacists dates back to 1618, when the first London Pharmacopœia was compiled. In 1826, Imperial measures and standards were legalized in England, and in 1827 exact copies of these standards were furnished the minister of the United States Government at London; namely, the standard yard, a bronze bar of 36 inches length, a brass troy-pound weight of 5760 grains, and a brass avoirdupois-pound weight of 7000 grains; copies of these standards were supplied to the different States in 1836 by Act of Congress. The length of the standard yard is determined by comparison with a pendulum beating seconds of mean time, in a vacuum, at the temperature of 62° Fahrenheit, at the level of the sea, in the latitude of London; the length of such a pendulum was found to be 39.13929 inches.

From what has been said above it is clear that every troy or apothecaries' ounce is heavier than the avoirdupois ounce by $42\frac{1}{2}$

$1\frac{17}{175} = 1.09714$

grains; hence to find the corresponding value in avoirdupois ounces of any given number of troy or apothecaries' ounces, add to the latter $\frac{42\frac{1}{2}}{437\frac{1}{2}} = \left(\frac{85}{875} \text{ or } \frac{17}{175}\right)$ of that number, thus ℥xxiv = 24 avoirdupois ounces plus $\frac{17}{175}$ of 24, which is 24 + 2.33, or 26.33 ounces; if, on the other hand, avoirdupois weight is to be converted into apothecaries' or troy weight, subtract from the number of ounces given $\frac{42\frac{1}{2}}{480} = \left(\frac{85}{960} \text{ or } \frac{17}{192}\right)$ of the number, thus 26.33 ounces $= 26.33 - \frac{17}{192}$ of 26.33, which is equal to 26.33 — 2.33, or 24 apothecaries' or troy ounces.

While apothecaries' weight is employed in compounding prescriptions both in this country and Great Britain, it is not used in either the United States or British Pharmacopœias, and will no doubt be entirely abolished in the course of time, when a uniform international system of weights shall have been adopted by the medical and pharmaceutical professions of both countries. The grain is the connecting link between avoirdupois, troy, apothecaries' and Imperial weight, being the same in all.

The fluid measure used by pharmacists of the United States is derived from the old wine measure of England (now extinct), which allowed to each wine gallon the volume of 231 cubic inches, or 58340.011 grains of distilled water at 15° C. (59° F.); the Imperial gallon of Great Britain contains 277.273 cubic inches, or 70,000 grains of distilled water at 62° Fahr. In both cases the gallon is divided into 8 pints, but the pint of wine measure contains 16 fluidounces, while the Imperial pint contains 20 fluidounces. The United States fluid measure has the following units: the minim, the fluidrachm, and the fluidounce, which are represented by the following signs: ♏, f℥, f℥; in addition, the pint and gallon are sometimes employed in commercial transactions, being designated by the abbreviations *O*, from *Octarius*, for pint, *Cong.*, from *Congius*, for gallon. The units of Imperial fluid measure bear the same names as those employed for United States fluid measure, but differ from them in value; thus, while the Imperial minim of water weighs 0.91 (0.9114583) grain, the United States minim of water weighs 0.95 (0.9493) grain, and, since both fluidounces contain 480 minims, the Imperial fluidounce of water weighs 437.5 grains, but the United States fluidounce 455.70 grains, at 15.6° C. (60° F.). Each fluidounce is divided into 8 fluidrachms and each fluidrachm into 60 minims.

It must not be overlooked that many liquids, although dispensed and sold by the apothecary by fluid measure, are purchased from the manufacturer by weight, and whenever the specific gravity of the liquid differs materially from that of water there must be also a

marked difference in the relative volume; thus glycerin, syrups, chloroform, ethers, acids, essential oils, and many chemical solutions, are always purchased by weight. The following list shows the number of fluidounces in one pound of the respective liquids, of pharmacopœial quality:

One Pound of	Sulphuric Acid measures about	. .	$8\frac{1}{2}$	fluidounces.
" "	Monsel's Solution measures about	. .	10	"
" "	Chloroform " "	. .	$10\frac{1}{4}$	"
" "	Syrup " "	. .	$11\frac{3}{4}$	"
" "	Glycerin " "	. .	$12\frac{1}{2}$	"
" "	Goulard's Extract " "	. .	$12\frac{1}{2}$	"
" "	Ammonia Water " "	. .	16	"
" "	Stronger Ammonia Water measures about		17	"
" "	Spirit of Nitrous Ether " "		$18\frac{1}{4}$	"
" "	Essential Oil measures from	. . 13 to	18	"
" "	Ether measures about	. . . .	$21\frac{1}{2}$	"

The METRIC or DECIMAL system of weights and measures, which is the only official system of the present United States Pharmacopœia, is supposed to have originated in the fertile mind of the French statesman, Prince de Talleyrand, toward the close of the last century, and was enforced in France by law in December, 1799. It has already become the legal standard in all civilized countries except the United States and Great Britain, and is destined to become the universal standard for commercial transactions, as it is already for strictly scientific work, the world over.

The use of metric weights and measures was legalized in the United States and Great Britain in 1866, but neither country has as yet officially adopted them, although the prospects for such desirable action are brightening. In 1878 the use of the metric system was made obligatory in the purchase of medical supplies for the United States Marine-Hospital service. Since the introduction of a new system of weights and measures must, no doubt, for a time create some confusion, a careful study of the same is required of pharmacists and physicians. The principles upon which the metric system was founded are as follows: The reduction of all weights and measures to one uniform standard of linear measure; the use of an aliquot part of the earth's circumference as such standard; the application of the unit of linear measure to matter in its three modes of extension—length, breadth, and thickness—as a standard of all measures of length, surface, and solidity; the cubic contents of linear measure in distilled water at the temperature of its greatest density to furnish at once the standard measure of weight and of capacity; everything susceptible of being weighed or measured to have only one measure of weight, one measure of length, and one measure of capacity, with their multiples and subdivisions exclusively in decimal proportions, and every weight and every measure to be designated by an appropriate significant characteristic name applied exclusively to itself.

As a basis, the authors of the metric system adopted a quadrant

(one-fourth) of the earth's circumference, and dividing this into ten million parts they obtained a certain measure of length, which they named METER (French *mètre*) and adopted as a standard for all units of measurements; this meter, which was made the unit of linear measure, is equal to 39.3704 inches. One-tenth part of the meter, applied to cubic measurement, was made the unit of measure of capacity and called a LITER (French *litre*); it is equal to 33.8149 U. S. fluidounces or 2.1135 wine pints. The one-thousandth part of the liter (which is equal to the cube of one-hundredth part of the meter) was chosen to furnish the unit of weight; the weight of such a volume of distilled water at its greatest density, 4° C. (39.2° F.), was called a GRAMME, and is equal to 15.43235639 grains. The multiples of these units are denoted by prefixes of the Greek numerals, *deka* 10, *hecto* 100, *kilo* 1000, *myria* 10,000; while prefixes of the Latin numerals denote the subdivisions, thus *deci*, one-tenth; *centi*, one-hundredth, and *milli*, one-thousandth. Two other units of the metric system, the *are* (the square of ten meters), and the *stere* (a cubic meter), are not of pharmaceutical interest. Although the liter is the unit of measures of capacity, the subdivisions of this unit are almost invariably spoken of as so many cubic centimeters, since each liter is equal to 1000 cubic centimeters, thus the expressions 10, 50, 100, 250, 750 cubic centimeters, etc., are preferred to 1 centiliter, 5 centiliters, 1 deciliter, one-fourth of a liter, and three-fourths of a liter. In like manner the specific names of the fourth multiple of the units are rarely employed, it being customary to designate all above the third multiple as so many of that multiple, thus 10 kilometers instead of 1 myriameter, 15,000 liters instead of 1½ myrialiter, and 20 kilogrammes instead of 2 myriagrammes, etc. When writing the names of metric measures and weights, abbreviations are usually employed in place of the full names, as will be seen from the following tables, which also give the corresponding values in customary weights and measures:

Measures of Length.

1 Myriameter,	Mm.	=	10000.0	M.	=	6.2137+	miles.
1 Kilometer,	Km.	=	1000.0	"	=	4.9710+	furlongs
1 Hectometer.	Hm.	=	100.0	"	=	19.8840+	rods.
1 Dekameter,	Dm.	=	10.0	"	=	32.8086+	feet.
1 Meter,	M.	=	1.0	"	=	39.3704	inches.
1 Decimeter,	dm.	=	0.1	"	=	3.93704	"
1 Centimeter,	cm	=	0.01	"	=	0.393704	"
1 Millimeter.	mm.	=	0.001	"	=	0.0393704	"

Measures of Capacity.

1 Myrialiter,	Ml.	=	10000.0	L.	=	2641 7890+	gallons.
1 Kiloliter,	Kl.	=	1000.0	"	=	264.1789+	"
1 Hectoliter,	Hl.	=	100.0	"	=	26.4178+	"
1 Dekaliter,	Dl		10.0	"	=	2.6417+	"
1 Liter,	L	=	1.0	"	=	33.8149+	fluidounces.
1 Deciliter,	dl.	=	0.1	"	=	3.38149+	"
1 Centiliter,	cl.	=	0.01	"	=	0.338149+	"
1 Milliliter,	ml.		0.001	"	=	0.0338149+	"
1 Cubic centimeter,	ccm.	=	0.001	"	=	0.0338149+	"

Measures of Weight.

1 Myriagramme,	Mg.	=	10000.0	G.	=	22.0461+ pounds.
1 Kilogramme,	Kg.	=	1000.0	"	=	2.2046+ "
1 Hectogramme,	Hg.	=	100.0	"	=	3.5273+ av. ozs.
1 Dekagramme,	Dg.	=	10.0	"	=	154.3235639 grains.
1 Gramme,	Gm.	=	1.0	"	=	15.43235639 "
1 Decigramme,	dg.	=	0.1	"	=	1.543235639 "
1 Centigramme,	cg.	=	0.01	"	=	0.1543235639 "
1 Milligramme,	mg.	=	0.001	"	=	0.01543235639 "

The U. S. Pharmacopœia deviates from these abbreviations in three instances, using *Mm.* in place of *mm.* for millimeter, *Cm.* in place of *cm.* for centimeter, and *Cc.* in place of *ccm.* for cubic centimeter. The numerical expression of all weights and measures should always be accompanied by the abbreviation used for the unit, and whenever subdivisions are not given a cipher should follow the decimal point, so as to indicate more clearly the intention of the writer; thus, 25.0 Gm. and 350.0 Cc., leave no doubt whatever as to the quantities desired, whereas 25 Gm. and 350 Cc. might have been carelessly written for 2.5 Gm. and 35.0 Cc. Since the value of the numerical expression depends entirely upon the correct placing of the decimal point, due care must be observed, lest the misplacement thereof increase or decrease the intended value tenfold. When reading metric weights and measures the multiples of the units should be read as so many units, but the subdivisions are preferably named as so many of the lowest division possible; for instance, 25.050 Gm. should be read 25 grammes and 50 milligrammes instead of 25 and $\frac{5}{100}$ grammes; 0.125 Gm., one hundred and twenty-five milligrammes instead of $12\frac{1}{2}$ centigrammes or 1 decigramme 2 centigrammes and 5 milligrammes; 0.02 M. should be read as 2 centimeters or 20 millimeters, but never as $\frac{2}{100}$ or $\frac{20}{1000}$ of a meter; 1.425 L. should be read as 1425 cubic centimeters instead of $1\frac{425}{1000}$ liter or 1 liter and 425 cubic centimeters.

The corresponding values, in customary weights and measures, of a few metric weights and measures should be firmly fixed in the mind for convenient use while reading or studying; as,

1 Mm. (millimeter) = $\frac{1}{25}$ of an inch.
1 Cm. (centimeter) = $\frac{2}{5}$ " "
1 inch = 25 millimeters or $2\frac{1}{2}$ centimeters.
1 Cc. (cubic centimeter) = 16.23 minims or 0.27 fluidrachm or 0.0338 fluidounce.
1 fluidounce = 29.57+ cubic centimeters at 4° C. (39.2° F.), or 29.53 Cc. at 15.6° C (60° F.)
1 Gm. (gramme) = 15.4324 grains.
1 grain = 0.06479+ gramme or 64.79 milligrammes.
1 Mg. (milligramme) = 0.01543 grain (practically $\frac{1}{65}$ grain).
1 L. (liter) = 33.815 (nearly 34) fluidounces or $2\frac{1}{8}$ pints.

In larger commercial transactions the kilogramme is the metric weight generally employed, being frequently abbreviated, "kilo"; it is equivalent to $2\frac{1}{5}$ avoirdupois pounds + 34 grains.

The following simple rules will enable anyone to readily convert metric weights and measures into those customary in this country, the results being practically correct.

For linear measure: Divide the number of millimeters by 25, 300, or 900; the quotients will be the answer in inches, feet, or yards, respectively.

For measures of capacity: Divide the number of cubic centimeters by 0.06163, 3.697, or 29.57; the quotients will be the answer in U. S. minims, fluidrachms or fluidounces, respectively.

For weight: Divide the number of grammes by 0.06479, 3.8874, or 31.0992; the quotient will be the answer in grains, drachms, or apothecaries' ounces respectively.

In the actual operations of weighing and measuring, however, it will be found more desirable to be provided with a set of accurate metric weights and measures; for then even the slight errors arising from the translation of one system into another can be avoided.

COMPARATIVE TABLE OF METRIC WITH AVOIRDUPOIS AND APOTHECARIES' WEIGHTS.

Names.	Numerical Expressions.	Equivalents in Grains.	Equivalents in Avoirdupois Weight.			Equivalents in Apothecaries' Weight.		
	Gm.	Gr.	lb.	oz.	gr.	℥	ʒ	gr.
Milligramme	0.001	0.01543	...	...	$\frac{1}{64}$	...	...	$\frac{1}{64}$
Centigramme	0.010	0.15432	...	...	$\frac{1}{8}$	...	...	$\frac{1}{8}$
Decigramme	0.100	1.54323	...	...	1.5	...	...	1.5
Gramme	1.0	15.43235	...	...	15.4	...	...	15.4
Dekagramme	10.0	154 32356	...	$\frac{1}{4}$	45.0	...	2	34.0
Hectogramme	100.0	1543.23563	...	$3\frac{1}{2}$	12.0	3	1	43.0
Kilogramme	1000.0	15432.35639	2	$3\frac{1}{2}$	10.47	32	1	12.4
Myriagramme	10000.0	154323.56390	22	$\frac{1}{2}$	14.8	321	4	3.5

The weight in grains of a cubic centimeter and a U. S. minim of distilled water must vary with the temperature at which the measurement is made; hence the relation between metric and U. S. apothecaries' fluid measure remains uniform for all temperatures. At 4° C. (39.2° F.) a cubic centimeter of distilled water weighs 15.4324 grains, while a minim weighs $\frac{1}{480}$ of 456.392 grains, or 0.9508 grain, hence each cubic centimeter is equal to 15.4324 ÷ 0.9508 or 16.23 minims; at 15° C. (59° F.) a cubic centimeter of distilled water weighs 15.392 grains, while a minim weighs 0.9483 grain, hence each cubic centimeter is equal to 15.392 ÷ 0.9483 or 16.23 minims.

In writing prescriptions, physicians are in the habit of considering 4 Cc. (actually 3.69969) as equivalent to 1 fluidrachm, and 30 Cc. (actually 29.57) as equivalent to 1 fluidounce.

COMPARATIVE TABLE OF METRIC AND APOTHECARIES' FLUID MEASURE

Cubic Centimeter.	Minims.	℥	ʒ	♏
0.06163	1.0	...	...	...
0.30815	5.0	...	...	...
0.61630	10.0	...	...	...
1.0	16.23	...	...	...
5.0	81.15	...	1	21.15
10.0	162.30	...	2	42.3
20.0	324.60	...	5	24.6
30.0	486.90	1	0	6.9
40.0	649.20	1	2	49.2
50.0	811.50	1	5	31.5
60.0	973.80	2	0	13.8
70.0	1136.10	2	2	56.1
80.0	1298.40	2	5	38.4
90.0	1460.70	3	0	20.7
190.0	1623.00	3	3	3.0
250.0	4057.50	8	3	37.5
500.0	8115 00	16	7	15.0
1000.0	16230.00	33	6	30.0

Physicians and pharmacists cannot be too careful in the use of metric weights and measures in the writing and reading of prescriptions. In continental Europe, where the metric system has been in use for many years, no signs are used in prescriptions, because all ingredients, whether solid or liquid, are weighed, and it is understood that weight is always intended; whenever, for any reason, measures are wanted, the signs L. (liter) or Ccm. (cubic centimeter) are employed. But in this country, and also in England, where it is still, and likely to remain, customary to weigh solids and to measure fluids in the dispensing of medicines, the official abbreviations given in the U. S. Pharmacopœia should be used invariably, so as to avoid all possible confusion; with water, and the average diluted alcohol tinctures, it would probably not make much difference whether grammes or cubic centimeters were dispensed, but in the case of all liquids having a higher or lower specific gravity than water, a marked variation will be observed; thus 20 Gm. of glycerin measure 16 Cc., and 20 Cc. of glycerin weigh 25 Gm.; 60 Gm. of simple syrup measure 45.5 Cc., and 60 Cc. of syrup weigh 79.02 Gm.; 30 Gm. of chloroform measure 20.13 + Cc., and 30 Cc. of chloroform weigh 44.7 Gm.; 4 Gm. of bromoform measure only 1.4 Cc., and 4 Cc. of bromoform weigh 11.32 Gm.; 10 Gm. of ether measure 13.77 + Cc., and 10 Cc. of ether weigh only 7.26 Gm.; 50 Gm. of alcohol measure 60.97 + Cc., and 50 Cc. of alcohol weigh 41 Gm.

It is incumbent upon the medical schools of this country to familiarize their students with the decimal system of weights and measures, as is now done in all colleges of pharmacy, and not until the National Medical and Pharmaceutical Associations shall have agreed upon some rule or guide for the two professions in the specification of metric weights and measures in prescriptions will the

pharmacist be relieved of annoyance and censure caused by an improper interpretation of quantities.

In the absence of specified fluid measures it is safest to follow the custom of continental Europe and weigh all solids and liquids when dispensing prescriptions written in the metric system.

In 1890 the United States Government obtained from the International Bureau of Weights and Measures prototype standards of the Meter and the Kilogramme, made of platinum-iridium; these were placed in the custody of the Office of Standard Weights and Measures at Washington, and from them the commercial weights and measures now in use are derived. The value of the United States prototype standard Meter and Kilogramme is identical with the international standards derived from the Mètre and Kilogramme "des Archives" of France.

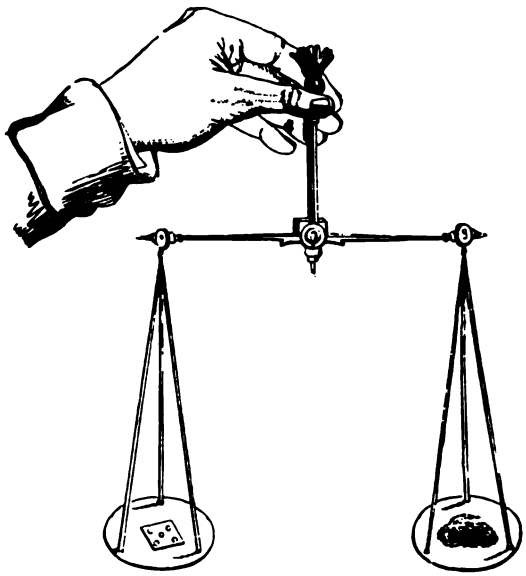
The United States yard is defined to be equal to $\frac{360000}{393700}$ of a meter; the pound (avoirdupois) is defined as being equal to $\frac{700000000}{1543235639}$ of a kilogramme, and the liquid gallon is the volume of 3785.434 grammes (58418.1444 grains) of water at the temperature of its maximum density, weighed in vacuo.

The instruments used in weighing and measuring are balances, weights, and graduated vessels, and the necessity for their accuracy and careful preservation cannot be too strongly emphasized.

THE BALANCE, or, as it is commonly called, "a pair of scales," is no doubt the most useful instrument in the hands of the pharmacist; upon its proper construction and sensitiveness depend the accuracy of weighing and correct dispensing of medicines; hence every well-equipped pharmacy should be supplied with at least three balances of different quality. The general construction of an ordinary balance is so well known to everybody that a detailed description seems unnecessary; the simple hand scales (see Fig. 1), which were formerly relied upon altogether, have almost completely disappeared in this country; in their stead a more substantial instrument is now used. The single beam principle still prevails, in which a metallic bar is supported at its centre on a knife-edged axis, called the fulcrum, thus producing two arms of equal length. The fulcrum projects from the sides of the beam, and rests on two supports at the top of a stationary column, so constructed that the wear and tear due to constant friction is relieved by a special contrivance for raising the beam above the steel or agate plane when the balance is not in actual use. The knife-edged axis and the support on which it rests are both made of hardened steel and highly polished, in order to reduce friction to a minimum; but, since even steel is liable to become rusty, particularly when exposed to moisture or acid vapors, agate edges and planes, which are practically indestructible, are now preferred on all finer

balances. The centre of gravity of the beam should be slightly below the edge of the fulcrum; if it were in the edge of the fulcrum, the beam would not come to a horizontal position when the pans are equally loaded, but would remain in any position where it might chance to be placed. If it were above the edge of the fulcrum, the beam would remain horizontal if placed so; but if slightly deflected it would tend to overturn by the action of the weight of the beam. The nearer the centre of gravity comes to the edge of the fulcrum, the more

FIG. 1.



Old-style hand balance.

accurate and sensitive it will be; but at the same time it will turn more slowly. The scale-pans are suspended in suitable wire frames also supported by means of knife edges from the ends of the beam; in order to insure perfect equilibrium it is essential that the end knife edges be situated equally distant from the central point of support and that they lie in the same plane with it, all three edges being parallel to each other. The lighter in weight and the more inflexible the beam the greater will be the sensitiveness of the balance. Both of these desirable qualities are obtained by the use of aluminum beams, which are also non-corrosive and non-magnetic.

The scale-pans are preferably made of solid nickel or solid silver; but for weighing certain chemical substances likely to attack the metal they should be supplanted by strong glass pans. Each balance is provided with an indicator in the form of a long, thin, flat needle attached to the centre of the beam and so arranged that

when the beam is in perfect stable equilibrium it points directly to the zero mark on a short graduated plate attached to the front base of the upright (see Fig. 2); on some balances the indicator points upward, the graduated scale being placed at a little distance above the beam (see Fig. 3.). When the balance is in use it is far better to rely upon the regular, uniform oscil-

FIG. 3.

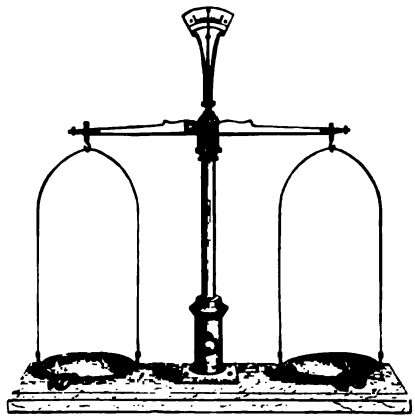
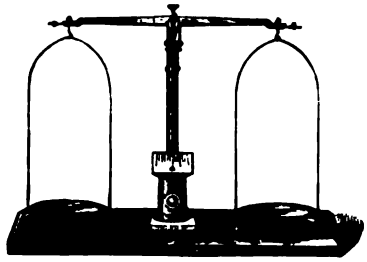


FIG. 2.



Prescription balance with indicator below the beam.

Prescription balance with indicator above the beam.

lations of the beam as shown by the indicator on the scale than to await the fixed position of the indicator at the zero point. Every balance when purchased should be carefully tested as to its sensibility and correct adjustment; this is best done by allowing the beam to oscillate freely supported on its fulcrum, with the pans detached. The oscillations should be regular and the beam finally return to its horizontal position of rest; but it must be borne in mind that an essential requisite for the success of this test is a perfectly level position of the balance. The equilibrium of the beam should also be maintained when the pans are attached, whether empty or lightly or heavily loaded, and when the load is transposed from one pan to the other; these tests prove equality in the length of the arms. Fine prescription balances should be kept enclosed in a suitable case provided with glass sides and top to protect them against dust, moisture, and corrosive vapors; they should not be scoured at any time, but simply polished with a piece of soft chamois skin or dusted with a soft camel-hair brush; under no circumstances should oil or chalk be used on the knife edges or planes.

Compound lever balances differ from those above described chiefly in having the pans situated above the beam and supported upon rods so constructed as to retain their vertical position during oscillation; they are less sensitive than the single beam prescription balances, and are generally used for coarser weighing. When enclosed in a box they are known as "box scales" and then possess

the advantage of having the more delicate parts of the mechanism protected against injury.

Fig. 4.

Prescription box scales.

Fig. 5.

Compound lever balance.

Figs. 4 and 5 show prescription and counter box scales constructed on the compound lever principle. Fig. 6 represents a convenient dispensing balance for rough prescription work, and is intended for quantities ranging from 30 grains to 2 or 4 ounces; it is sensitive to ½ grain, and is provided with a beam graduated into apothecaries' and metric weight (1 to 120 grains and 0.1 to 8.0 Gm.) and carrying a sliding poise.

Fig. 6.

Troemner's dispensing scale.

Special balances for weighing liquids, particularly in the laboratory, have been found very convenient on account of their peculiar construction. Fig. 7 represents Troemner's new solution balance, capable of weighing from 10 grammes to 16 kilogrammes (154 grains to about 36 pounds). The scale is provided with an extra balancing beam by which an empty bottle or container is quickly balanced by simply sliding the balance weight along until a correct balance is secured. A new system of adjusting weights, known as the ball system, is attached, and is a great improvement over the old method of using separate weights; small weights are adjusted on

the graduated beam in front, while the larger weights are represented by different positions of the balls on the central plate.

Since 1882 great improvements have been made in what are known as *torsion balances*. The chief difference between torsion and ordinary balances is the entire absence of knife edges and the location of the centre of gravity above the fulcrum or point of

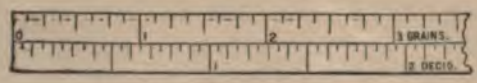
FIG. 7.

Troemner's new solution balance.

rotation. The knife edges have been replaced by thin steel springs stretched tightly between bearings, the centre of the beam being fastened to the centre of the strained spring and at right angles to it; under this condition the beam, by the elasticity or torsion of the

FIG. 8.

Torsion prescription balance.



Section of rider beam for same.

spring, will vibrate precisely as the ordinary beam balanced on knife edges. The pans rest upon similar torsion springs at the ends of the beam in the same manner as the central fulcrum of the beam. The inherent torsional resistance to oscillation, due to the tightly-stretched wire bands, is overcome by elevating the centre of gravity above the fulcrum, by means of a weight, to such a height that its tendency to reach its lowest position (vertically below the centre of rotation) almost neutralizes the total resistance. If, consequently,

the tendency of the high centre of gravity and the resistance of the wire bands are opposed to such an extent as to nearly neutralize each other, the sensitiveness of the balance is established, and the slightest weight placed on the pans will cause the beams to oscillate; on the other hand, the beams will return to their horizontal position by the unneutralized resistance. The foregoing principle has been applied to a variety of balances adapted for ordinary commercial weighing, as well as the more delicate adjustment of fine prescription work and chemical analysis; like ordinary balances they are provided with graduated beams and poise to be used in place of weights. Fig. 8 represents a torsion prescription balance of fine

FIG. 9.

Torsion counter scale in glass case.

Section of triple rider beam for same.

adjustment, with all the parts enclosed in a glass case and fully exposed to view; it is sensitive to 1 milligramme or $\frac{1}{64}$ of a grain, and up to 500 milligrammes or 8 grains all weights can be adjusted by means of a rider on the graduated beam. Fig. 9 represents a torsion counter balance sensitive to 2 grains, and having a capacity of 20 pounds; it is also provided with a triple graduated beam for avoirdupois, troy, and metric weights.

Every pharmacist who lays claim to doing even a moderate prescription business should have in his possession at least two balances, one of which may be used for weighing quantities ranging from 30 grains to 2 or 3 ounces, and should be sensitive to at least $\frac{1}{2}$ grain; while the other should be confined to quantities never greater than 2 grammes or 30 grains, and should respond readily to a change in weight amounting to 2 or 3 milligrammes or $\frac{1}{30}$ to $\frac{1}{20}$ grain; besides these a larger balance (usually termed counter scales) is needed for general trade; this should be of such adjustment as to allow accurate weighing thereon of quantities ranging from $\frac{1}{2}$ ounce

to 5 or 10 pounds, and should be sensitive to 5 or 10 grains, with a full charge.

WEIGHTS are pieces of metal designed to weigh aliquot parts of the established units; brass or iron is used for the customary commercial weights, while brass or aluminum is chosen for weights employed for dispensing purposes; platinum is also occasionally used for small prescription weights on account of its extreme hardness and resistance to atmospheric influences. Accurate weights are as essential as accurate balances, for one is rendered unreliable without the other. The usual form of commercial weights at present is in sets known as box or block weights and ranging from one-quarter ounce to five pounds (Fig. 10). Troy weights as a mark of distinction from avoirdupois weights are usually sold in nests of brass cups (see Fig. 11); they run from one-eighth ounce to eight or sixteen ounces, and for use in dispensing prescriptions the lower denominations, from ¼ grain up to 2 ounces, are frequently put up in boxes or blocks as shown in Fig. 12. The smaller dispensing weights are either made of brass or nickel-silver, after the style shown in Fig. 13, or of aluminum if below the

FIG. 10.

Block weights.

FIG. 11.

Set of apothecaries' cup weights.

FIG. 12.

Apothecaries' weights (½ gr. to ʒij) in case.

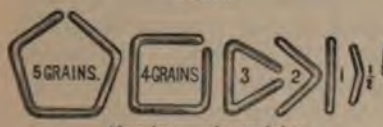
FIG. 13.

Brass or silver-nickel prescription weights.

denomination of ten grains (see Figs. 14 and 15); weights less than one-quarter grain are often indicated by means of a sliding poise on a graduated beam. The relative lightness of aluminum adapts this metal admirably for use in weights of very

low denominations, as they can be made of larger size and consequently be more conveniently handled than heavier brass weights. Metric weights are made of iron, brass, or aluminum, in the same forms as already described for avoirdupois and apothecaries' weight.

FIG. 14.



Aluminum wire weights.

FIG. 15.

Aluminum grain weights.

In connection with the operation of weighing, the term *tare* is frequently used to indicate the weight of the empty vessel (dish, box, bottle, or jar), in which the substance (liquid or dry) is to be weighed; *gross weight* is the combined weight of the substance and the container, *net weight* is the weight of the substance alone,

FIG. 16.

Set of metric prescription weights. (100 grammes to 1 centigramme.)

obtained by subtracting, from the *gross weight*, the *tare* of the container. Instead of finding the exact weight of the container, the latter may be simply *counterpoised* or balanced by small shot or dry coarse sand contained in a suitable cup.

Everyone who has occasion to use fine balances should early accustom himself to certain habits of care and neatness, which will materially preserve the sensitiveness of the instrument. The following rules are recommended: *Never allow the beam to oscillate when the balance is not in use. Immediately after the operation of weighing is completed, replace the weights in their proper receptacle and clean the pans with a soft towel. Never weigh deliquescent salts, or active chemicals, such as iodine, on the metal pans, but always on glass,*

or in tared vessels. Always weigh potent or poisonous drugs on stiff glazed paper, using two pieces of equal size to counterpoise each other. Never place large weights on the pans, or remove them, while the beam is in motion; this is easily accomplished by means of levers for keeping the beam and pans at rest.

MEASURES are vessels used for determining the volume of liquids, and even dry substances; the latter kind do not concern the pharmacist, who is compelled, however, to have on hand a variety of vessels suitably provided with appropriate scales of measurement for liquids. Such vessels are usually made of glass and are known simply as graduates; they occur of different capacities from 1000 cubic centimeters (1 liter) down to 5 cubic centimeters, and from 64 fluid-ounces down to 60 minims. The *Phenix and Acme Graduates*, manufactured in this country, are guaranteed to be accurate and made strictly according to the American standard of apothecaries' fluid measures; since Imperial measure differs materially from U. S. fluid measure, graduates made in England cannot be used in this country, unless they have been adjusted according to the American standard. Very accurate metric graduates are also now made in this country.

Graduates of different shapes are in use, conical, tumbler-shape, and cylindrical (see Figs 17, 18, 19), the last named of which,

FIG. 17.

Conical graduate.

FIG. 18.

Tumbler-shape graduate.

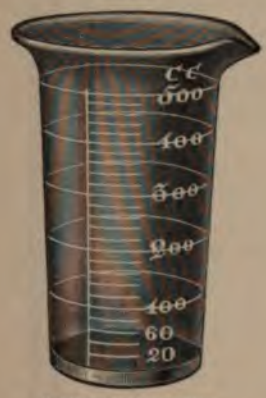
FIG. 19.

Cylindrical graduate.

although the most accurate, are but rarely seen in stores. Cylindrical graduates have a small diameter, which is uniform throughout the height of the vessel; hence errors in measurement due to capillary attraction are in these reduced to a minimum. For ¼ and ½ oz. graduates the diameter is about ½ inch; for 1 and 2 oz. sizes it should not exceed ¾ inches; while for the 4 oz. size, 1¼ inch diameter

will be ample. For measuring quantities less than two fluidounces the cone-shaped graduates will be found preferable to the tumbler-shape, but difficulty is often encountered in cleaning them properly, particularly the smaller sizes. The "Acme" graduates, introduced a few years ago, possess the advantage of being made flat on the bottom, without a foot, and hence are less liable to be upset or broken; they are admirably adapted for laboratory work, are cylindrical in form, of about the same diameter as tumbler-shape graduates, and can be had for both metric and apothecaries' fluid measure. (See Figs. 20 and 21.)

FIG. 20.



Metric fluid measure.

FIG. 21.

U. S. fluid measure.

Acme graduates.

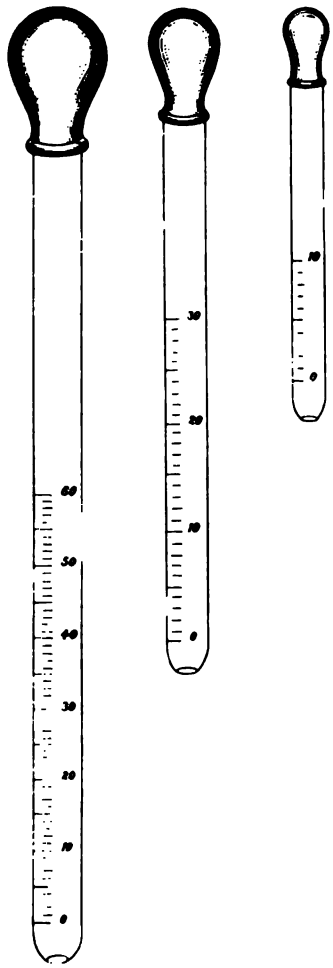
Duplex graduates, arranged for apothecaries' fluid measure on one side and metric fluid measure on the other, are not to be recommended, on account of the danger of confusion and the greater difficulty of accurate measurement.

Although minim graduates are extensively employed for measuring volumes of less than one-fourth fluidounce, it will be found more desirable to use minim pipettes (see Fig. 22) for quantities ranging from 5 to 60 minims; these instruments, first suggested by Dr. E. R. Squibb, are very accurately made and will be found extremely convenient. For measuring small metric volumes the graduated cubic centimeter pipettes of Dr. Curtman will be found very serviceable (see Fig. 23); they come in different sizes—5 and 10 and 25 Cc. capacity—each cubic centimeter being divided into tenths, and are especially adapted to pharmacopœial testing.

As to the proper manner of holding a graduate while measuring liquids, it may be said that the firmest hold is obtained by grasping the graduate with the left hand in such a manner that the first or index finger encircles the lower part of the vessel, the thumb resting on the base and the second finger forming a support by being placed under the base; this leaves the third and fourth fingers free to remove

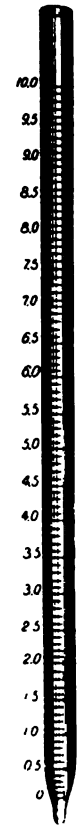
and hold the stopper of a bottle from which any liquid is to be measured; the mark to which the liquid is to be measured should be on a level with the operator's eye while the graduate is held in an upright position. Owing to capillary attraction, every liquid contained in a

FIG. 22.



Dr. Squibb's minim pipettes.

FIG. 23.



Dr. Curtman's cubic centimeter pipette.

graduate will present two concave surfaces, neither of which can be taken as the true level; hence a correct reading of the graduation can only be had by fixing the desired marking of the scale intermediate between the upper and lower edges of the liquid.

Graduates which have the same scale marked on both sides, or which are encircled by the markings of the scale, admit of more

accurate measurements and do not require that careful attention to levelling the graduate necessary with the plainer varieties.

Glass graduates are best cleaned by washing with a mop, using soap and water if necessary, rinsing with clear water and allowing the graduate to drain, either on a perforated tray or by hanging in a rack, but never should a towel be used to dry the graduate, as it is apt to leave lint adhering to the glass.

APPROXIMATE MEASUREMENTS. Owing to the varied density of liquids, the number of drops contained in a certain volume must vary greatly with different liquids; moreover the size of a drop is influenced by the size and shape of the vessel from which the drop is allowed to fall—so that a drop is a very uncertain quantity in the division of doses of medicines. The variability of adhesion to glass exhibited by different liquids as well as the rapidity with which liquids are allowed to flow from vessels, are other factors which determine the size of drops, as is shown in the case of chloroform.

Instead of being identical with the minim, drops may vary from one-fifth to one and one-fourth minim.

For the purpose of better illustration, the following short table has been inserted, showing the great variability in size of drops of different liquids:

TABLE SHOWING THE NUMBER OF DROPS TO A FLUIDRACHM.

Liquid.	120 minims Phenix Graduate.	1 fluidounce Phenix Graduate.	W. T. & Co's. exact Medicine Dropper.	Pint or Quart Shelf Bottle.
Distilled Water	48	46	128	
Tincture of Aconite . . .	150	150	190	120
" " Belladonna . .	144	144	174	108
" " Chloride of Iron .	150	150	190	120
" " Opium . . .	130	130	154	
" " " Camphorated	136	136	170	
" " Deodorized Opium .	90	110	124	80
Glycerin	90	76	90	
Purified Chloroform . . .	234	240	304	160
" " second trial	274	279	360	180
Dil. Hydrocyanic Acid . .	60	80	75	60 (℥j bottle)

For the administration of medicines certain familiar domestic measures are employed, which, although subject to considerable variations, are usually estimated as having the following capacity:

A teaspoonful, equal to one fluidrachm;
A dessertspoonful, equal to two fluidrachms;
A tablespoonful, equal to one-half fluidounce;
A wineglassful, equal to two fluidounces;
A teacupful, equal to four fluidounces; and
A tumblerful, equal to eight fluidounces.

Figs. 24, 25, and 26 represent convenient medicine glasses, well adapted for family use.

FIG 24. FIG. 25. FIG. 26.

Graduated medicine glasses.

These vessels are now obtainable, accurately graduated and made to correspond to apothecaries' fluid measure—hence they are preferable to the variable tea-, dessert- and tablespoons generally met with, and should be employed altogether in the sick-room.

CHAPTER III.

SPECIFIC GRAVITY.

A KNOWLEDGE of the subject of specific gravity is of importance to the pharmacist, as it frequently enables him to detect impurities or to determine the identity and quality of the drugs he handles. Specific gravity means relative weight, or the relation between the volume and weight of bodies as compared with a standard—the standard for liquids and solids being distilled water, while atmospheric air or hydrogen is used for gaseous bodies; in other words, specific gravity is the ratio between the weight of any gaseous, liquid, or solid body and that of an equal volume of the respective standard.

The principle of specific gravity was first announced by Archimedes, a Greek philosopher, who formulated the law that all bodies immersed in a liquid are buoyed up with a force equal to the weight of the liquid displaced by them; hence a piece of metal of the size of one cubic inch, when immersed in water, will exert as much less pressure on the bottom of the container as will equal the weight of one cubic inch of water—or a fraction over 252 grains. Floating bodies always displace their own weight of water, irrespective of their volume, while immersed bodies always displace their own volume of water, irrespective of their weight; hence all bodies whose volume weighs less than an equal volume of water are sure to float, only so much of the body being immersed as equals a like weight of water, while all bodies whose volume weighs more than an equal volume of water must sink and be completely immersed, as this downward pressure of the body exceeds the upward pressure or buoyant force of an equal volume of water.

As the volume of all bodies varies with temperature, it is essential that the comparison of weights be made at some fixed temperature and that equal volumes of the standard and body examined be weighed at the *same* temperature. In some countries the temperature of 4° C. (39.2° F.), at which pure water assumes its greatest density, is taken for the comparison of weights, while in the United States and German Pharmacopœias, 15° C. (59° F.) has been fixed, with very few exceptions, as the normal temperature; the British Pharmacopœia has selected 15.6° C. (60° F.). As the comparison of weight of equal volumes of bodies may be made at any temperature desired or convenient, and as the specific gravity will vary accordingly, it is necessary to state the temperature in connection with specific gravity; for instance, to say that a liquid has the

specific gravity 1.42, would not indicate at what temperature the liquid had been weighed, nor would it indicate comparison with water at the same temperature—hence the ratio would be an uncertain expression; to say that a liquid has the specific gravity 1.42 *at* 15° *C.*, would still leave a doubt as to the temperature at which an equal volume of pure water had been weighed for comparison, for it may have been 4° C., 12° C., or even 25° C., and, in either case, the specific gravity named would not be absolutely correct; to say, however, that a liquid has the specific gravity 1.42 *at* 15° *C. as compared with water at the same temperature*, leaves no room for doubt as to the true ratio existing between the liquid and water—it therefore expresses the true specific gravity. The United States Pharmacopœia (1890) expressly states that all of its specific gravities are to be considered as taken at 15° C and *compared with water at the same temperature*, whenever no special temperature is mentioned.

As it is frequently more convenient to weigh substances at a temperature above 15° C. than to cool the substance down and keep it at that point, the average room-temperature, 22° C. (71.6° F.), or even 25° C. (77° F.), has been suggested by some authorities, and will often be found preferable.

Barometric pressure is not without effect on the relation between the volume and weight of bodies, hence absolute specific gravity, like absolute weight, is only obtainable *in vacuo;* for pharmaceutical purposes this difference is always ignored and the barometric pressure assumed to be normal, 760 Mm. or 30 inches.

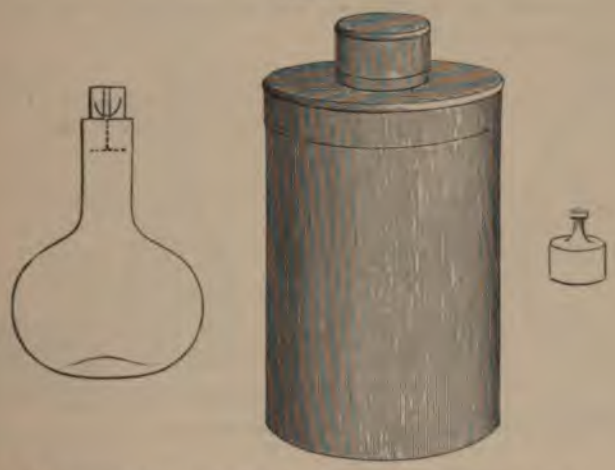
The specific gravity of a solid or liquid is always expressed by a number which shows how often the weight of a certain volume of water is contained in the weight of the same volume of that solid or liquid; and the specific gravity of a gaseous body is expressed by a number which shows how often the weight of a certain volume of atmospheric air (or hydrogen) is contained in the weight of the same volume of that gaseous body. The specific gravity of water is therefore stated to be 1, and the specific gravity of air (or hydrogen) is likewise stated to be 1. The following simple rule may be given for finding the specific gravity of any liquid or solid substance by calculation: Divide the weight of a given volume of any liquid or solid by the weight of an equal volume of distilled water, both weighings having been made at the same temperature. The quotient expresses the specific gravity.

Specific Gravity of Liquids.

The determination of the specific gravity of liquids is far more frequently required than that of solids. The different instruments employed for that purpose are specific gravity flasks or pycnometers, loaded glass cylinders, specific gravity beads, and specific gravity spindles or hydrometers. Any small flask, of 25 or 50 Cc. capacity, with a long, narrow neck and made of thin glass, will answer as a

specific gravity bottle. Its weight, or tare, is first carefully ascertained and noted; pure water is then poured into the flask until it reaches a short distance up into the neck, when a mark should be made with a file at the upper and lower edge of the meniscus or concave surface; having noted the temperature of the water, the flask and contents are weighed, and from it the tare of the flask is deducted, the remainder being the weight of that particular volume of pure water at the given temperature. The tare, temperature and weight of water, are carefully etched on the side of the flask, which is now ready to be used for taking the specific gravity of any liquid, by filling it to the mark in the neck with the liquid to be tested, then weighing and dividing the net weight of the liquid by the weight of the water, the quotient being the specific gravity of the liquid. Suppose the flask weighs 324 grains and holds, up to the mark, 647 grains of water; filled to the mark with sulphuric acid, it weighs 1511.5 grains, which leaves $1511.5 - 324 = 1187.5$ grains as the weight of the acid. Now applying the rule, to divide the weight of a given volume of a liquid by the weight of the same volume of water, the specific gravity is found to be $1187.5 \div 647 = 1.835+$.

FIG. 27.



Glass-stoppered specific gravity bottle with tin case and counterpoise.

Small glass-stoppered flasks, graduated to hold 100, 250, 500, or 1000 grains of distilled water at 15.6° C. (60° F.), are a more convenient form of pycnometer; they come packed in tin cases and are accompanied by a metal counterpoise to balance the empty bottle (see Fig. 27). In using these flasks it is necessary to fill them with the liquid to be tested, to a little above the mark in the neck to which the glass stopper reaches when inserted, so that the air and small excess of liquid shall be forced out through the capillary tube

drilled through the stopper. The liquid to be tested, having the same temperature as that at which the flask has been adjusted, may be weighed, after wiping the flask dry, when, in the case of the 100 or 1000-grain bottle, the weight at once expresses the specific gravity, by simply placing the decimal point correctly, without further calculation; for, as the weight of water (100 or 1000 grains) is to the weight of the same volume of any liquid, so is the specific gravity of water (1.000) to the specific gravity of that liquid. Example: If the 100-grain bottle be found to hold 141.5 grains of a certain acid, the specific gravity of that acid will be 1.415; for 100 : 141.5 : : 1.000 : x. $x = 1.415$.

For the general purposes of the pharmacist, the above-described specific gravity bottles give results sufficiently accurate, the most annoying practical difficulty lying in the proper adjustment of the temperature. At certain seasons of the year the prescribed temperature of 15° or 15.6° C. is readily attained; but in summer, when the temperature of the atmosphere frequently reaches 32° C. (89.6° F.) and over, the dew-point rises above 15.6° C. and moisture is deposited on the outside of the cooler bottle while weighing, thus sensibly increasing its weight. The following table, taken from Parrish's *Treatise on Pharmacy*, was compiled by Dr. W. H. Pile, and is based on the corrections made for contraction and expansion of the 1000-grain bottle used, as well as the water:

TABLE OF APPARENT AND TRUE SPECIFIC GRAVITY OF WATER AS OBSERVED IN A GLASS BOTTLE AT DIFFERENT TEMPERATURES.

Temp. Fahr.	Sp. Gr. in Glass Bottles.	True Sp. Gr.	Temp. Fahr.	Sp. Gr. in Glass Bottles.	True Sp Gr.
50°	1000.54	1000.67	72°	998.94	998.78
51	1000.50	1000.62	73	998.83	998 66
52	1000.46	1000.56	74	998.72	998 53
53	1000.41	1000.50	75	998.60	998.40
54	1000.36	1000.44	76	998.48	998.27
55	1000.30	1000.37	77	998 35	998.13
56	1000.25	1000.30	78	998.22	997.99
57	1000.20	1000.23	79	998.08	997.84
58	1000.14	1000.16	80	997.94	997.68
59	1000 07	1000.08	81	997.79	997.52
60	1000.00	1000.00	82	997.64	997.36
61	999.92	999.91	83	997.49	997.20
62	999.84	999.82	84	997.35	997.04
63	999.72	999.72	85	997.20	996.87
64	999.68	999.63	86	996.94	996.60
65	999.60	999.53	87	996.78	996.43
66	999.51	999 43	88	996.62	996.26
67	999.42	999.33	89	996.46	996.08
68	999.33	999.23	90	996.29	995.90
69	999.24	999.12	91	996.12	995.72
70	999.14	999.01	92	995.96	995.54
71	999.04	998.90	93	995.79	995.36

With a view of overcoming the difficulties usually encountered and of insuring more accurate results, Dr. E. R. Squibb has had constructed a set of specific gravity bottles which are equally well adapted to all standards of temperature from 4° C. to 25° C. (39.2° F. to 77° F.) (See Fig. 28.) By means of the long narrow tube stopper, graduated into half-millimeters, the volume of liquid in the bottle is capable of very accurate adjustment. When first adjusted, the zero mark on the scale indicates the point to which the volume of the

FIG. 28.

standard weight of recently boiled distilled water reaches at 4° C., while the upper limit of the scale indicates the volume at 25° C. Since glass bottles contract appreciably for two years or more after they have been made, the graduations should be verified every six months or more until contraction has ceased, a memorandum of the changes being kept for reference when the bottle is to be used; thus the point for the volume at 4° C. may have advanced from 0 to 2 or 3 divisions of the scale, and similarly for any temperature volume. The bottles are always used in a bath of either warmed

or cooled water, and when the volume does not change for five minutes, as indicated by the graduated scale, the contents of the bottle may be known to have assumed the temperature of the bath as ascertained by means of a delicate thermometer. A leaden collar is used to keep the bottles steady in the bath, and the adjustment of volume is made by means of a fine pipette and blotting paper.

Besides taking the specific gravity of liquids by means of a pycnometer, accurate results may be obtained with the so-called loaded cylinder; its use is far less troublesome, and as it can be employed at any temperature between 4° and 40° C. (39.2° and 104° F.) it requires less careful attention to the adjustment of the latter. The loaded cylinder, as shown in Fig. 29, consists of a glass tube partly filled with mercury and sealed at the top, to which is affixed a hook for convenient suspension to a scale beam. Having weighed the cylinder in air and then in pure water, at any given temperature, the weight of an equal volume of water is ascertained by subtracting the weight in water from the weight in air; the cylinder is then weighed in any desired liquid at the same temperature as the water, and the loss in weight again noted, which is the weight of an equal volume of that liquid. The volume of the liquid to be tested, being equal to the volume of the cylinder, must be equal to the volume of water also, for things that are equal to the same thing are equal to each other; by dividing the weight of the given volume of the liquid by the weight of the same volume of water, the specific gravity of the liquid is obtained. Example: A loaded cylinder weighs in air 150 grains, and in water 120 grains, loss of weight in water 30 grains; weighed in sulphuric acid it weighs 96 grains, showing a loss of 54 grains; equal volumes of the acid and water weighing 54 and 30 grains respectively, the specific gravity of the acid must be 1.800, for $54 \div 30 = 1.8$.

Fig. 29.

Loaded cylinder.

Fig. 30.

Glass or metal plummet.

When only a small quantity of liquid is available for taking the specific gravity the loaded cylinder may be replaced by a small glass or platinum weight of the shape shown in Fig. 30; or Grauer's method may be followed. This consists in using a small pipette having a fine orifice at one end, and at the upper end a short piece of rubber tubing closed by a pinchcock; a mark is made on the glass stem, showing the height to which a convenient quantity of water rises (say 1.0 Gm. or 1.0 Cc.), and enough of the liquid to be tested is drawn up through the tube to the mark previously made, the tube is closed, and the whole then weighed; the weight of the liquid in grammes expresses the specific gravity with sufficient accu-

DR. O. G. FREYERMUTH

racy for all practical purposes, as water increases its volume from 4° to 100° C. only to the extent of 0.012, or about $\frac{1}{84}$.

The principle of the loaded cylinder has been utilized in the construction of the Mohr specific gravity balance, of which the Westphal modification is a most desirable improvement (see Fig. 31). The specific gravity of a liquid can be quickly taken at any temperature between 7° and 30° C., since the loaded cylinder has been replaced by a short glass thermometer, which is suspended from the

Fig. 31.

The Westphal specific gravity balance.

end of the beam by a thin platinum wire; the adjustment having been made at 15 C., a slight variation will be observed for any higher or lower temperature. The small thermometer has a range of twenty-three degrees on the Centigrade scale, and, when suspended in air from the longer arm of the beam, establishes perfect equilibrium; when completely immersed in distilled water at 15° C. it displaces its own volume of the water and is buoyed up by a force equal to the weight of the water displaced—equilibrium of the beam being re-established by attaching the necessary counterpoise, which

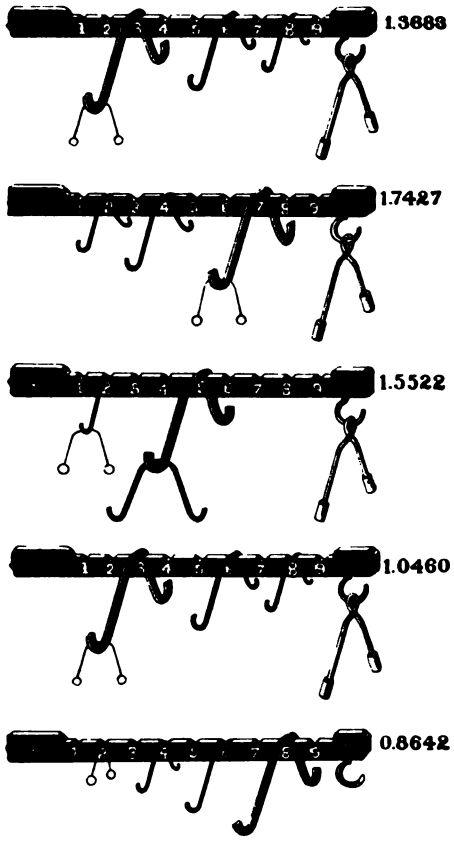
is called 1.000: at 7.5° C. the necessary weight was found to be 1.001, while at 27° C. it was 0.998. As seen in the illustration, the longer arm of the beam is accurately divided into ten even spaces, and the weights, or riders, used to counterbalance the thermometer when immersed in any liquid, are made of brass and aluminum; they are so constructed that each smaller rider is of exactly $\frac{1}{10}$ the value of the next larger, the largest rider and the counterpoise used to balance the thermometer in water, however, being of the same weight or value. Without the necessity for calculation, if the temperature of the liquid be at 15° C., the specific gravity of the liquid can be at once read off, after the equilibrium of the beam has been established; for instance, in testing alcohol at 15° C., the counterpoise necessary to balance the beam in water will be found too heavy if attached at the same point in alcohol, hence it is removed, and the largest rider is placed in the first, or, if necessary, in the second notch on the beam, where it may appear a little too light, and then the smaller riders are added as may be necessary to balance the beam perfectly. The value of each of the two larger riders, when suspended from the end of the beam, is considered as 1.000, while the three smaller riders are valued at 0.100, 0.010, and 0.001 respectively; when removed to the top of the beam the value of each rider is reduced by $\frac{1}{10}$ for every notch. If one of the large riders be placed at the notch marked 8, a second rider at 2, and a smaller rider at 1, the specific gravity of the alcohol must be read as 0.821. In the case of chloroform and all other liquids specifically heavier than water the large counterpoise is suspended from the end of the beam, and the other riders are placed in the notches as may be necessary; thus chloroform may require all four riders on the beam, the largest at 4, the second at 8, and the smaller two at 9, which would be read as 1.489 specific gravity. Whenever two riders of different weight are required in the same notch on the beam, the lighter of the two is suspended from the hook of the heavier, as shown in Fig. 32; thus the specific gravity of liquids can be read with accuracy to four decimal places. The Mohr or Westphal balance cannot be used, however, if only very small quantities of liquid are available, as sufficient liquid is required to immerse the glass thermometer completely.

Specific gravity beads, also known as Lovi's beads, are small, sealed, pear-shaped glass bulbs of various specific weights, which have been carefully ascertained and are marked on them; these beads will float indifferently in any liquid having the same specific gravity, and may be used in reducing liquids to a fixed specific gravity by dilution or evaporation. If a bead marked 0.93 be placed in a jar of alcohol it will sink—unless the liquid happens to be official diluted alcohol—but will slowly rise upon the addition of water, until a sufficient quantity has been added to increase the specific gravity of the mixture to that indicated on the bead, when it will float about midway in the liquid. Results obtained

with specific gravity beads are never so accurate as with other methods.

Hydrometers, or areometers, are instruments intended to indicate either the density or specific gravity of liquids, and in some cases also the percentage by volume or weight of certain liquids. They

FIG. 32.



Showing the manner of reading the specific gravities.

consist of a glass tube having a bulb blown at one end, a little above which the tube is usually expanded cylindrically for a short distance, and then terminates in a long stem in which is securely fastened a graduated paper scale (see Fig. 33). The bulb is filled with mercury or small shot, so as to enable the instrument to assume a vertical position when floated in any liquid. Hydrometers, like all floating bodies, displace their own weight of a liquid and sink in it to a depth proportional to the volume of liquid displaced, which volume is equal in weight to the weight of the instrument; thus, by

comparison of volumes displaced, the densities and specific gravities of various liquids can be ascertained. While the great majority of hydrometers are so constructed that with constant weight they will sink to varying depths in different liquids, some are made to sink to a uniform depth in all liquids by the addition or subtraction of weights, and the density, or specific gravity, is calculated from such change of weight; this latter class can also be conveniently used for taking the specific gravity of solids.

Fig 33.

Hydrometer plain.

Specific gravity hydrometers are made with the unit mark 1.000 at a point to which the instrument sinks in distilled water at *normal temperature* (usually 15.6° C. or 60° F.), and then have the scale carried above and below this point, each mark on the scale indicating either 0.001, or 0.005, or 0.010, according to the intended delicacy of the instrument. As specific gravities of liquids range from 0.700 to above 2.00, the tube of a hydrometer carrying such a scale would have to be inconveniently long to permit of a fair reading of it; hence specific gravity hydrometers usually come in sets of four, ranging from 0.600 to 1.000, from 1.000 to 1.400, from 1.400 to 1.800, and from 1.800 to 2.200. When intended for testing the specific gravity of special liquids the scale is usually much shorter, and thus permits of more accurate graduation.

By far the larger number of hydrometers are intended for determining the density of liquids irrespective of specific gravity; they are extensively employed for technical purposes and are based on arbitrary scales, no two of which agree, but which can be converted into specific gravity by certain rules. To this class belong Baumé's, Twaddell's, Cartier's, Zanetti's, Sikes', Beck's, Jones' and other hydrometers. Since Baumé's hydrometers are largely used by manufacturing chemists in this country, and the *degrees Baumé* are often stated on labels, the instrument is of special interest to pharmacists.

Baumé had two hydrometers, one for liquids heavier than water and the other for liquids lighter than water; the former was called *Pèse-Acide*, or *Pèse-Sirop*, and the latter *Pèse-Esprit*. For liquids heavier than water the zero was placed at the point to which the instrument sank in distilled water at 15.6° C., and the point to which it sank in a solution of 15 parts of dry table salt and 85 parts of distilled water, also at 15.6° C., was marked 15; the distance between these two points was then divided into 15 equal parts, called *degrees*, and the scale extended as far as the length of the tube would permit. The zero for liquids lighter than water was found by immersing the instrument in a solution of 10 parts of dry table

salt and ninety parts of distilled water at 15.6° C. in such a way that the long stem would be almost entirely out of the liquid; the point to which the instrument sank in distilled water, also at 15.6° C., was marked at 10, the space between the two points being divided into 10 equal parts and the scale extended as in the other case. The slightest error in obtaining the first interval is increased upon extension of the scale; hence it is almost impossible to find two instruments adjusted by the old method to correspond exactly. A more accurate and equally practicable method is to obtain the exact specific gravity of two liquids compared with distilled water at a fixed temperature, place these at the extremes of the scale, and then divide the intervening space into the requisite number of degrees. The liquids chosen in this country, for liquids heavier than water, are concentrated sulphuric acid having the specific gravity 1.8354 at 15.6° C., and distilled water; and for liquids lighter than water, highly rectified ether having the specific gravity 0.725 at 15.6° C., and distilled water; the space between the points to which the hydrometer sinks in the water and the acid is divided into 66 parts, or degrees, and the space between the points to which it sinks in the ether and the water into 53 parts. For all liquids heavier than water the scale is read from above downward, while for liquids lighter than water it is read from below upward. (See Figs. 34 and 35.)

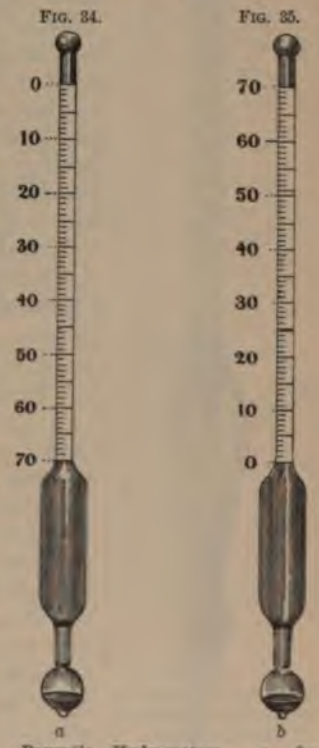
As it is frequently desirable to know the specific gravity for any given degree on the Baumé scale, and *vice versa*, the following rules have been formulated.

For liquids heavier than water: Subtract the degree Baumé from 145 and divide the remainder into 145 to find the specific gravity.

Divide 145 by the specific gravity and subtract the quotient from 145 to find the degree Baumé.

For liquids lighter than water: Add the degree Baumé to 130 and divide the sum into 140 to find the specific gravity.

Divide 140 by the specific gravity and from the quotient subtract 130 to find the degree Baumé.



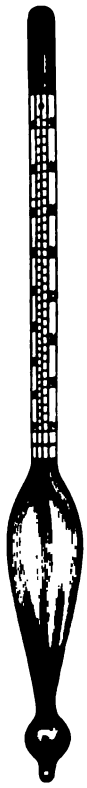
Baumé's Hydrometers. *a*, for liquids heavier than water; *b*, for liquids lighter than water.

The moduli or constants employed in these rules express the proportion which the weight of water displaced by the hydrometer when

floating in water bears to the weight of water equal in bulk to one degree. Thus, if a Baumé hydrometer be floated in water at 0 on the hydrometer for heavier liquids, or at 10 on the hydrometer for lighter liquids, it will require the addition of $\frac{1}{145}$ of the weight of the hydrometer to sink it one degree in the first case, or the withdrawal of $\frac{1}{140}$ of its weight to allow it to rise one degree in the second case. The fact that the water-line is marked at 10 instead of 0, on Baumé hydrometers for liquids lighter than water, necessitates the use of 130 instead of 140 in the foregoing rule.

In order to avoid the use of rules and tables in connection with arbitrary scales, hydrometers have been in use for some years bearing a double scale, for Baumé degrees and the corresponding specific gravity, as shown in Fig. 36: they come in sets, usually five, two of which are intended for liquids lighter than water, and three for liquids heavier than water, the shorter size permitting closer reading within smaller limits.

FIG. 36.

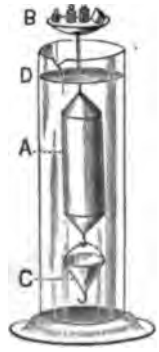


Double hydrometer for density and specific gravity determinations.

The Twaddell hydrometer is only for liquids heavier than water, each degree on the scale being equal to 0.005 specific gravity; hence the requisite number of degrees multiplied by 0.005 and added to 1.000 expresses the specific gravity of any liquid; thus, if a sample of glycerin stands at 50° Twaddell, its specific gravity will be 1.250, for $50 \times 0.005 = 0.25$ and $1.0 + 0.25 = 1.25$.

Nicholson's and Fahrenheit's hydrometers are of the kind intended to sink to a uniform depth (indicated by a mark on the stem) in all liquids, by the use of weights. Fig. 37 represents a Nicholson hydrometer floating in a liquid. The construction is readily explained: A is an elongated glass or metal bulb, terminating in a stem surmounted by a metallic disk, B; on the stem is a mark at D, indicating the point

FIG. 37.



Nicholson's hydrometer.

to which the instrument must be made to sink, and attached to the bottom of the bulb by means of a small hook is a loaded cup, C, for carrying solids if so desired. When the hydrometer is immersed in water, sufficient weights are placed on the disk, B, to cause the instrument to sink to the point D; it is then transferred to the liquid to be tested, and the weights adjusted as before; the weight necessary to sink the hydrometer to the proper point represents the weight of the volume of liquid displaced by it; hence the weight necessary in the case of any liquid, divided by the weight required in the case of water, gives the specific gravity of that liquid.

Fig. 38.

Alcoholometer with thermometer enclosed.

Spirit hydrometers, usually called alcoholometers, are used to ascertain the percentage of absolute alcohol in the commercial article; since the value of alcohol depends entirely upon the amount of absolute alcohol present, this instrument is a most desirable piece of apparatus for pharmacists. Alcoholometers are made of glass, like ordinary hydrometers, but of much longer shape, and are usually provided with two separate scales—Richter's scale, indicating the percentage of alcohol by weight, and Tralles' scale, showing the percentage by volume; since the instrument is adjusted at 15.6° C. (60° F.) it becomes necessary to make proper corrections for any variations in temperature. When immersed in alcohol at normal temperature the figures on the respective scales to which the instrument sinks indicate the number of parts of absolute alcohol contained in 100 parts of the specimen, the lowest mark on the scale being 0, to which the hydrometer will sink in pure water. Since a cold temperature, by contraction, increases the density of alcohol the instrument cannot sink so low in the liquid if the temperature be below 15.6° C. as when normal; an additive correction in the reading of the scale must therefore be made. On the other hand, if the temperature rise above 15.6° C. the density of the alcohol will decrease and the hydrometer will sink lower, hence a subtractive correction must be made for temperature. The necessary correction has been ascertained to amount to 0.27 of 1 per cent. for every degree on the Centigrade scale, or 0.15 of 1 per cent. for every degree on the Fahrenheit scale. For example, if an alcoholometer sinks in alcohol to 93° on the Tralles' scale at 50° F. (10° C.), the liquid contains really

94.5 per cent. of absolute alcohol by volume, instead of 93 as indicated on the scale, for the temperature is 10° Fahrenheit below the normal, hence 10 × 0.15, or 1.5, must be added: but if the temperature had been 70° F. (21.11° C.) the true percentage of alcohol by volume would have been only 91.5, for, the temperature being 10° above normal, a subtraction of 1.5 from the reading 93 is necessary. Fig. 38 represents a complete alcoholometer carrying a thermometer within the tube for convenience in taking the temperature of the liquid. For testing the specific gravity of urine a small hydrometer the range of which extends from 1.000 to 1.060 is employed (see Fig. 39); the narrow cylinder in which to float the urinometer

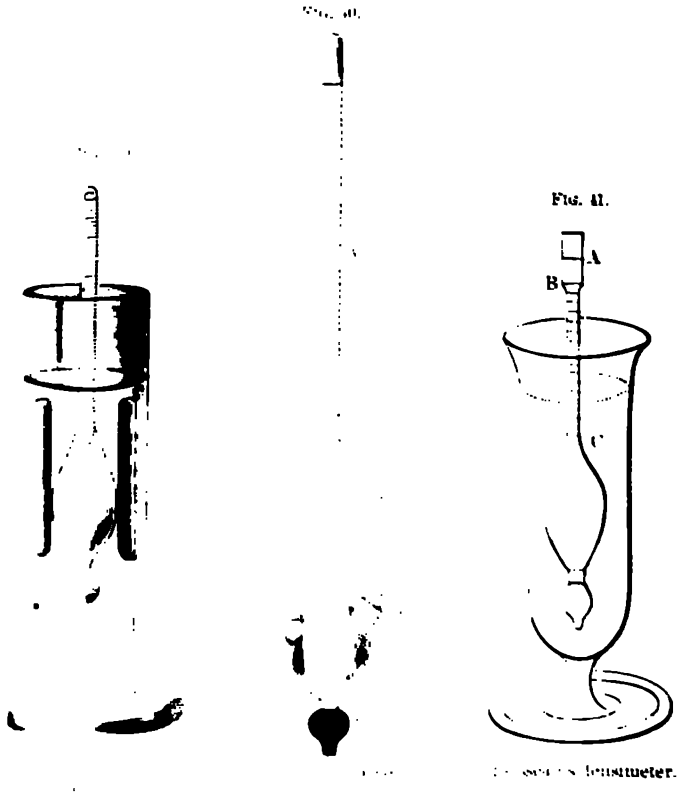


Fig. 40.

Fig. 41.

[illegible] densimeter.

[illegible] the view of preventing the [illegible] means of the peculiar [illegible]

[illegible] the specific gravity [illegible] Eichhorn's areo-pyenometer [illegible] (Fig. 41) instead of

floating these instruments in the liquid to be tested, the latter is carried in the hydrometer, which is then floated in water. The illustration of the areo-pycnometer shows that it differs in construction from the ordinary hydrometer chiefly in having a glass bulb, C, placed between the loaded bulb, F, and the expanded portion, B, of the stem; the bulb C is provided with a stopcock, D, and into it is poured the fluid to be tested; the small glass knob, E, serves to balance the instrument when immersed in water, which should be at 17.5° C. (63.5° F.); the specific gravity is shown on the divided scale in the tube, A. The densimeter is chiefly intended to be used for oils and similar liquids lighter than water. The upper part of the tube, A to B, consists of a little cup of 1 Cc. capacity; when floated in water the instrument sinks to the point C, and when carrying 1 Cc. of water in the cup it sinks to B. The space on the stem between B and C is divided into 20 equal parts, each division corresponding to $\frac{1}{20}$ Gm. or 0.050 Gm.; now, if 1 Cc. of oil of peppermint be poured into the cup and the instrument floated in water it will probably sink to the eighteenth division of the scale—hence $18 \times 0.05 = 0.900$, the specific gravity of the oil.

Specific Gravity of Solids.

The various methods for finding the specific gravity of solids are based upon the well-established principles that all bodies immersed in a liquid displace a quantity of that liquid equal in volume to the volume of the body immersed, and at the same time are buoyed up with a force equal to the weight of the liquid displaced. The upward pressure exerted by the liquid upon the body immersed causes the latter to appear lighter in weight, and is proportional to the density of the liquid; the loss of weight, then, which a body seems to suffer upon immersion in any liquid, represents the weight of a volume of that liquid identical with the volume of the body immersed. As stated on page 45, pure water at 15.6° C. (60° F.) has been chosen as a standard of comparison for solids, and may be directly employed for the immersion of all bodies upon which no solvent effect is produced; in the contrary case, other liquids must be used, as will be shown later on. The specific gravity of any solid can be ascertained by the simple rule of three, provided the first three terms of the proportion are known, namely: first term, the weight of the liquid displaced; second term, the weight of the solid in air; third term, the specific gravity of the liquid used for immersion. Whenever water is used for immersion, the simple division of the weight of the solid in air by the loss of weight in water (weight of water displaced) expresses the specific gravity of the solid, since the specific gravity of water is 1.000. The methods for finding the specific gravity of solids may be divided as follows:

1. For solids insoluble in, but heavier than water;
2. For solids insoluble in, but lighter than water;

3. For solids soluble in water, whether heavier or lighter than that liquid;

4. For solids in powder form.

For solids insoluble in, but heavier than water, several methods are available; of these, the direct method of weighing is the most accurate and generally employed.

In place of the more expensive hydrostatic balance, any good sensitive prescription balance may be used; the only extra piece necessary being a small wooden or stiff wire bench as a support for the vessel of water, as shown in Fig. 42. For instance, a piece of

FIG. 42.

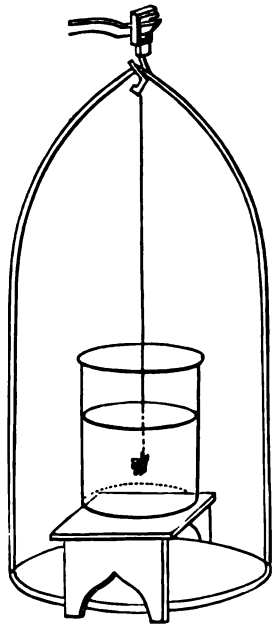
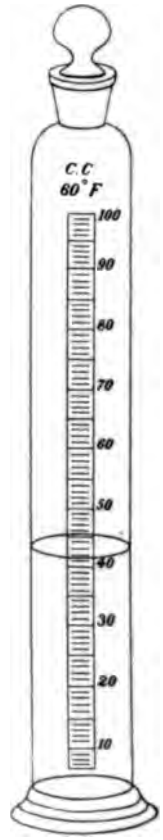


Diagram showing the manner of weighing a solid body in a liquid.

FIG. 43.



Graduated cylinder.

metal is found to weigh 258.75 grains in air; by means of a silken thread, or fine horse-hair, it is completely immersed in pure water and found to weigh 235.75 grains, the difference or loss of weight, 23 grains, representing the weight of a volume of water equal in volume to the 258.75 grains of metal. Dividing 258.75 by 23, the specific gravity of the metal is found to be 11.25.

Another but less accurate method is to weigh the solid in metric weight and then place it in a graduated cylinder containing sufficient water to submerge the solid completely (see Fig. 43); the difference between the first height of the water and that after immersion of the

solid indicates the volume of water displaced, and its corresponding weight is readily noted. Suppose a solid body weighing 7.5 Gm., placed into 40 Cc. of water, causes the latter to rise to 41.5 Cc., showing that 1.5 Cc. of water have been displaced, which weigh 1.5 Gm.; then, applying the rule, $7.5 \div 1.5 = 5$, the specific gravity of the solid.

Since solid bodies will float indifferently in any liquid having the same specific gravity as themselves, advantage may be taken of this property to determine the specific gravity of solids. Hager recommends determining the specific gravity of fats by placing them in alcohol and then adding water until the fat floats about indifferently beneath the surface of the mixture; the specific gravity of the mixture is then taken in the usual way, preferably by means of a pycnometer, and this at the same time expresses the specific gravity of the solid.

To ascertain the specific gravity of solids insoluble in, but lighter than water, it becomes necessary to insure their immersion in water by attaching to them some heavy substance, the weight of which in water must previously have been ascertained. Upon immersing the two bodies in water it will be observed that the weight of the two appears less than the weight of the heavy body alone, which is due to the fact that the volume of water equal to the volume of the lighter body is heavier than the latter, and therefore exerts a greater upward pressure on the heavy body, causing it to appear to lose weight. The difference between the weight of the heavy body in water and the united weight of the light and heavy bodies in water expresses the excess of weight of a volume of water over the weight of a like volume of the light body; in other words, it shows how much heavier a volume of water is than the same volume of the light body; to find the exact weight of a volume of water equal to the volume of the light body, this difference, or excess, must be added to the weight of the light body in air. Suppose a piece of cork weighs 62.5 grains in air; attached to a piece of metal which weighs 94 grains in water, the whole is found upon immersion in water to weigh 88 grains, or 6 grains less than the metal alone; adding 6 to 62.5 grains (the weight of the cork) we obtain 68.5 grains, the weight of the water displaced by the cork. The specific gravity of the cork is found by dividing 62.5 by 68.5 according to the general rule on page 46. The answer will be 0.9124+.

For solids soluble in water some other liquid must be selected for immersion, in which the solid body is perfectly insoluble and of which the specific gravity is known; in other respects any of the preceding methods may be followed. In such cases the weight of the liquid displaced, having been ascertained, may be used to find the weight of a corresponding volume of water, and the latter then be divided into the weight of the solid; or the weight of the solid in air may be divided by the weight of the liquid displaced and the quotient then multiplied by the specific gravity of the liquid; by either

method the specific gravity of the soluble substance will be obtained. To find the weight of a corresponding volume of water, divide the weight of the liquid displaced by its specific gravity, for the weights of equal volumes of two bodies are to each other directly proportional as their specific gravities. Example: A piece of alum weighs 125 grains in air; immersed in oil of turpentine having the specific gravity 0.860 it weighs 62 grains; 125 divided by 63 (the loss of weight) yields 1.984; oil of turpentine weighing only 0.86 as much as water, 1.984 must be multiplied by 0.860, which gives 1.7062+ as the specific gravity of the alum. Or the weight of a volume of water corresponding to the volume of oil of turpentine displaced may be found by dividing 63 by 0.86, which equals 73.256, and this divided into 125, the weight of the alum in air, also gives 1.7062+ as the specific gravity of the alum.

Sometimes it is desirable to find the specific gravity of solids in powder form, as calomel, reduced iron, lead oxide, and the like; this is best done by using a flask or bottle known to hold a definite quantity of water, introducing a certain weight of the powder, and then filling with water and weighing the total contents; as two bodies cannot occupy the same space at the same time, it follows that the flask or bottle containing the powder cannot hold the same quantity of water as when empty, and this difference corresponds to the weight of water equal in volume to the powder. Suppose 100 grains of an insoluble powder are placed in a counterpoised 1000-grain bottle, the latter being then filled with pure water; if the total contents weigh 1088 grains, 12 grains of water have been displaced by the powder, for 1088 — 100 leaves 988, and, as the bottle is capable of holding 1000 grains of water, the difference 1000 — 988 = 12 must have been displaced. Then applying the rule, 8.333+ is found to be the specific gravity of the powder, as 100 ÷ 12 = 8.333+.

Specific Volume.

The term specific volume is used to define the ratio existing between the volumes of certain weights of bodies and the volume of the same weight of pure water; it is therefore the opposite of specific gravity. Specific volume is ascertained by dividing the specific gravity of a body into unity, and hence may be called the reciprocal of specific gravity; it may also be found by dividing the weight of a given volume of water by the weight of an equal volume of a liquid. Every pharmacist is aware that it will require vessels of different size to hold one pound of ether, water, glycerin, sulphuric acid, oil of turpentine, or chloroform, and it is often desirable to know in advance the volume of a given weight of a liquid; the weight in grammes of any liquid multiplied by the specific volume, or divided by the specific gravity, of that liquid at once expresses the actual volume in cubic centimeters. To find the volume of a given weight, avoirdupois or apothecaries', of a liquid, it becomes necessary

first to ascertain the volume of a like weight of water, and then to multiply this by the specific volume, or to divide by the specific gravity of the liquid; or the given weight of a liquid may be divided at once by its specific gravity, which will yield the weight of a volume of water equal to the volume of the liquid, and then by finding the volume of such a weight of water the volume of the liquid is at once known.

Examples: If the volume of 500 Gm. of alcohol U.S.P. is desired, divide 500 by 0.820, the specific gravity of the alcohol, and the quotient 609.75+ will be the answer in cubic centimeters.

To find the volume of 8 ounces of official glycerin (apothecaries' weight) it is necessary to multiply by 480, the number of grains in 1 ounce, and then divide the product by 455.7, the number of grains in one U. S. fluidounce of water, the quotient ($480 \times 8 = 3840$; $3840 \div 455.7 = 8.427$), 8.427, represents the number of fluidounces contained in the same weight of water; 8.427 then divided by 1.25, the specific gravity of the glycerin, yields 6.7416 fluidounces as the volume of 8 troy ounces of glycerin.

How large a bottle is required to hold one pound of chloroform of 1.490 specific gravity? One pound avoirdupois is equal to 7000 grains, and $7000 \div 1.490 = 4697.986$, the weight in grains of a volume of water equal to the chloroform; then $4697.986 \div 455.7 = 10.309$, or very nearly $10\frac{1}{2}$ fluidounces.

Adjustment of Specific Gravity and Percentages.

While the adjustment of percentages in liquids as well as solids presents no difficulties, the reduction of liquids from a higher to a lower specific gravity is not quite so easily accomplished, since specific gravity is but the expression of the relation between volume and weight, and condensation of volume frequently occurs as the result of a mixture of two liquids. Two very simple rules, or formulas, have been published for the adjustment of specific gravities of liquids, by volume and by weight; but absolutely accurate results are only possible when *no contraction* of volume takes place; in the majority of cases the condensation of volume is but very slight, and for ordinary purposes may be ignored. It is well known that the weights of equal volumes of two liquids are to each other directly proportional as the specific gravities of these liquids; therefore, the weight of a liquid divided by its specific gravity represents a weight of water equal in volume to the weight of that liquid. It is also well known that the volumes of equal weights of two liquids are to each other inversely proportional as the specific gravities of these liquids; therefore, the volume of a liquid multiplied by its specific gravity represents a volume of water equal in weight to the volume of that liquid. The well-known process of *alligation* is admirably adapted to the adjustment of specific gravities of liquids by volume, but is unsuited to adjustment by weight. When two liquids of

different specific gravities are mixed, the loss which one suffers will be balanced by the gain of the other; hence, the two liquids used must be mixed in inverse proportion to that existing between the gain and loss of specific gravity and the specific gravity of the mixture; the difference between the higher specific gravity and the desired specific gravity of the mixture will therefore indicate the proportion of the liquid having the lower specific gravity; and the difference between the lower specific gravity and the desired specific gravity will indicate the proportion of the liquid having the higher specific gravity. For example, if solution of ferric chloride, specific gravity 1.520, is to be reduced to 1.387 specific gravity by addition of a weaker solution of 1.280 specific gravity, 107 volumes of the stronger must be mixed with 133 volumes of the weaker solution, or, in other words, 1 volume of the former with 1.243 volumes of the latter. It is customary to set down a problem in alligation in the following manner to facilitate comparison:

$$1.387 \begin{cases} 1.520 \mid 0.107 = \text{proportion of the stronger liquid.} \\ 1.280 \mid 0.133 = \text{proportion of the weaker liquid.} \end{cases}$$

If a definite volume of the mixture is desired, the requisite volume of the stronger and weaker liquids may be ascertained by dividing the desired volume by the sum of the proportionals, and then multiplying each proportional by the quotient so obtained; thus, if 32 fluidounces are wanted, divide 32 by 0.240 (0.107 + 0.133), which yields 133.3; 0.107 × 133.3 = 14.27 fluidounces, the requisite volume of the stronger solution, and 0.133 × 133.3 = 17.73 fluidounces, the requisite volume of the weaker solution.

To adjust the specific gravity of a given weight of a liquid to a higher or lower specific gravity, the following formula may be employed:

$$x = \frac{w \times c\,(a - b)}{a\,(b - c)}$$

in which x represents the weight of the diluent, w the weight of the liquid to be diluted, a the specific gravity of the liquid to be diluted, b the desired specific gravity, and c the specific gravity of the diluent. (Whenever water is the diluent, c is made 1.000.) As stated before (see page 63), $\frac{w}{a}$ = weight of water equal in volume to w, $\frac{x}{c}$ = weight of water equal in volume to x, $\frac{w + x}{b}$ = weight of water equal in volume to $w + x$. To find the value of x, the following equation, $\frac{w}{a} + \frac{x}{c} = \frac{w + x}{b}$, must be solved:

$$wcb + abx = wac + acx$$
$$abx - acx = wac - wcb$$
$$x \times a\,(b - c) = w \times c\,(a - b)$$
$$x = \frac{w \times c\,(a - b)}{a\,(b - c)}$$

Example: How much water must be added to 250 Gm. of solution of potassa of 1.539 specific gravity in order to reduce the specific gravity to 1.036? Substituting numerical values for the letters

$$250 \times 1.000(1.539 - 1.036)$$

1129 GUERRERO STREET
BETWEEN 23D AND 24TH

HOURS: 1 TO 4 AND 7 T
SUNDAYS BY APPOI
TELEPHONE CONNEC

RESIDENCE: 1133 GUERRERO STREET

SAN FRANCISCO, _____

_____

_____

TO **DR. O. G. FREYERMUTH,** DR.

FOR PROFESSIONAL SERVICES RENDERED

TO _____ TO DATE, $ _____

RECEIVED PAYMENT.

_____

STATEMENTS RENDERED

Examples: Reduce 4 pints (64 fluidounces) of 93 per cent. (by volume) alcohol to 65 per cent.: $64 \times 93 = 5952$, and $5952 \div 65 = 91.57$. Enough water must be added to the 4 pints of alcohol to yield, after contraction has ceased, 91.57 fluidounces.

Reduce 2 pounds of hydrochloric acid from 31.9 per cent. to 10 per cent.: 2 pounds = 32 avoirdupois ounces; $32 \times 31.9 = 1020.8$, and $1020.8 \div 10 = 102.08$. Enough water must be added to the 2 pounds of acid to bring the total weight up to 102.08 avoirdupois ounces.

Reduce 8 troy ounces of stronger ammonia water, 28 per cent., to 10 per cent. strength: $8 \times 28 = 224$, and $224 \div 10 = 22.4$. Enough water must be added to the 8 troy ounces of stronger ammonia water to bring the total weight up to 22.4 troy ounces.

For making a definite quantity of a solution of a certain percentage by diluting a stronger solution with water: *Multiply the required quantity by the required percentage, and divide by the higher percentage; the quotient will be the quantity of the stronger liquid necessary, and this subtracted from the total quantity required leaves the necessary quantity of water.* When volume adjustment of alcohol is made, the same precautions in regard to contraction of volume must be observed as stated in the preceding rule.

Examples: Make 1 gallon (128 fluidounces) of 60 per cent. (by volume) alcohol from alcohol of 94 per cent. (by volume): $128 \times 60 = 7680$, and $7680 \div 94 = 81.7$. Answer: 81.7 fluidounces of the stronger alcohol must be mixed with sufficient water to yield, after contraction has ceased, 128 fluidounces.

Make 4 pounds of 25 per cent. phosphoric acid from the official 85 per cent. acid: 4 pounds = 64 av. ozs.; $64 \times 25 = 1600$, and $1600 \div 85 = 18.823$. Answer: Enough water must be mixed with 18.823 av. ozs. of the strong acid to bring the total weight up to 64 av. ozs.

Make 720 grains of 5 per cent. caustic potash solution from a 12.5 per cent. solution: $720 \times 5 = 3600$, and $3600 \div 12.5 = 288$; $720 - 288 = 432$. Answer: 288 grains of the 12.5 per cent. solution must be mixed with 432 grains of water.

The adjustment of percentage in liquids may also be readily made by the process of alligation, as already explained under adjustment of specific gravities by volume, page 64.

Pharmacists and drug jobbers are sometimes called upon to make mixtures of certain liquids or solids having different percentage strengths in order to produce a desirable average strength; this may be done by the general rule for alligation. Write the percentages in a column, and the mean percentage on the left. Connect the simples in pairs, one less than the mean with one greater; take the difference between the mean and the numbers representing the percentage strength of each simple and write it opposite the value with which it is linked. These differences are the relative quantities of the simples taken in the order in which their values stand.

Example: In what proportion must powdered opium of 9, 12.5, 15, and 16 per cent. morphia strength be mixed to produce a mixture of 14 per cent. strength?

				Proof.					Proof.
	9.0	1.0	1 × 9	= 9		9.0	2.0	2 × 9	= 18
14	12.5	2.0	2 × 12.5	= 25	or 14	12.5	1.0	1 × 12.5	= 12.5
	15.0	5.0	5 × 15	= 75		15.0	1.5	1.5 × 15	= 22.5
	16.0	1.5	1.5 × 16	= 24		16.0	5.0	5 × 16	= 80
		9.5		) 133			9.5		) 133.0
				14					14

Answer: 1 part of 9 per cent., 2 parts of 12.5 per cent., 5 parts of 15 per cent., and 1.5 parts of 16 per cent., or 2 parts of 9 per cent., 1 part of 12.5 per cent., 1.5 parts of 15 per cent., and 5 parts of 16 per cent.

It matters not how the simples are connected, as long as one less than the mean is compared with one greater, for while the proportional part of each simple may vary, the sum of the proportionals remains the same. If the number of simples is not evenly divided among those less and those greater than the mean, two or more of the former may be linked with one of the latter, and *vice versa;* thus, to mix 7, 8, 9, and 28 per cent. ammonia water so as to produce 10 per cent. ammonia water, it would be necessary to use 6 parts of the 28 per cent. solution and 18 parts each of the 7, 8, and 9 per cent. solutions.

			Proof.
	7	18	18 × 7 = 126
10	8	18	18 × 8 = 144
	9	18	18 × 9 = 162
	28	3 + 2 + 1 = 6	6 × 28 = 168
			60) 600
			10

If a definite quantity of one of the simples be directed to be used in the mixture, the corresponding quantities of the others are readily ascertained by multiplying their proportionals by the ratio which the given quantity bears to the proportional of the simple which it represents.

Example: How much powdered cinchona bark containing 3, 3.5, 6, and 6.5 per cent. total alkaloids must be mixed with 10 pounds of cinchona bark containing 4 per cent. total alkaloids to produce a mixed powder of official strength, 5 per cent. total alkaloids.

10 ÷ 1 = 10, ratio of given quantity to proportional.

	3.0	1.5
	3.5	1.5
5	4.0	1.0
	6.0	1.0
	6.5	2.0 + 1.5 = 3.5

Answer.		Proof.
1.5 × 10 = 15	pounds of 3 % bark.	15 × 3 = 45
1.5 × 10 = 15	" " 3.5 " "	15 × 3.5 = 52.5
1.0 × 10 = 10	" " 4 " "	10 × 4 = 40
1.0 × 10 = 10	" " 6 " "	10 × 6 = 60
3 5 × 10 = 35	" " 6.5 " "	35 × 6.5 = 227.5
		85) 425.0
		5

If a definite quantity of a mixture is required, the quantity of each simple may be ascertained by multiplying its proportional by the ratio which the total quantity required bears to the sum of the proportionals of all the simples.

Example: How many grammes of powdered opium of 9, 12, 15, 16, and 17 per cent. morphia strength must be taken to produce 250 grammes of a mixture containing 14 per cent. of morphia.

	9	3 + 2 = 5	5 × 13.89 = 69.45
	12	1	1 × 13.89 = 13.89
14	15	2	2 × 13.89 = 27.78
	16	5	5 × 13.89 = 69.45
	17	5	5 × 13.89 = 69.45
		18 the sum of proportionals	250.02

250 ÷ 18 = 13.89, ratio of required quantity to the sum of the proportionals.

Answer: 69.45 Gm. each of 9 per cent., 16 per cent., and 17 per cent. opium, 13.89 Gm. of 12 per cent. opium, and 27.78 Gm. of 15 per cent. opium.

The foregoing rule can also be applied to a mixture of liquids of different specific gravities.

Example: A pharmacist is called upon to prepare 500 Cc. of a mixture of alcohol, spec. grav. 0.820; glycerin, spec. grav. 1.25; simple syrup, spec. grav. 1.317; and water; the mixture to contain 15 per cent. by volume of glycerin, and to have the same specific gravity as water. How will he proceed?

The 500 Cc. of mixture must weigh 500 Gm. in order to have the same specific gravity as water; 15 per cent. of 500 is 75, and 75 Cc. of glycerin of 1.25 specific gravity will weigh 93.75 Gm.; this leaves 425 Cc. as the volume of the alcohol, syrup, and water mixture, the weight of which must be 500 — 93.75 = 406.25 Gm. Such a mixture would have the specific gravity 0.9559, for 406.25 ÷ 425 = 0.9559, and the necessary quantity of each ingredient may be ascertained by alligation, thus

	0.820	0.0441 ÷ 0.3611 = 0.4052	proportional of alcohol.
0.9559	1.000	0 1359	" " water.
	1.317	0 1359	" " simple syrup.
		0.6770	sum of the proportionals.

425 : 0.6770 = 627.8, ratio of required quantity to the sum of the proportionals.

627.8 × 0 4052 = 254.384 Cc. of alcohol.
627.8 × 1 359 = 85.318 Cc. of water.
627.8 × 1 359 = 85.318 Cc. of syrup.

Cc.		Proof.		
254.384	@	0.820	=	208.594
85.318	"	1.000	=	85.318
85.318	"	1.317	=	112.363
75.000	"	1.250	=	93.750
500.020			)	500.025 (1.000

Answer: 75 Cc. of glycerin must be mixed with 85.318 Cc. each of simple syrup and water, and 254.384 Cc. of alcohol. No allowance has been made for contraction of volume, which is sure to follow; hence the final volume of the mixture will be slightly below 500 Cc. and the specific gravity slightly above 1.000.

CHAPTER IV.

HEAT.

ONE of the most valuable aids to the pharmacist in the numerous manipulations of the store and laboratory is HEAT; hence a knowledge of its varied application and the modes of controlling and directing its influence is necessary.

The undulatory theory regarding heat is now accepted by all scientists; this declares heat to be a force generated by the motion of the molecules of bodies, and that it is the increase or decrease of this molecular energy that gives rise to the conditions designated as *hot*, *warm*, and *cold*. No body is entirely without motion of its molecules, hence the terms heat and cold are merely relative; moreover different bodies have different capacities for heat, as is clearly proven by two persons entering the same apartment, one of whom may complain of uncomfortable warmth, while the other experiences a chilly sensation. The chief effect of heat, or increased molecular motion, is to overcome the force of cohesion and expand the volume of bodies by increasing the intermolecular spaces; the three states of aggregation, known as solid, liquid, and gaseous, being the result of cohesive force, are, therefore, dependent upon the amount of heat generated in or applied to a body.

All solid bodies, when their molecular motion has become sufficiently intensified, will become luminous, as is shown by the spark emitted when steel and flint are struck together, or by the kindling of flame when two pieces of dry wood are rubbed together vigorously for some time.

Oftentimes the luminosity of heated bodies is used to indicate the degree of heat exhibited; hence such terms as dull-red heat, cherry-red heat, and white heat, of which the first named is produced during ordinary combustion of fuel in a stove, without a strong draught of air, while the last-named is the result of most intense activity in molecular motion, brought about by the aid of a powerful air-blast in the combustion of fuel or by the use of electric currents.

Heat may be either active or latent; the former increases the temperature of bodies and causes their expansion, while the latter is heat hidden, after the expansion has been effected, for the purpose of keeping up the expansion. Active or sensible heat can be measured by its effect on mercury, upon which latent heat makes no impression; the latter can be converted into the former, however, by pressure and other agencies.

Heat is in almost daily use by the pharmacist in the operations of

solution, fusion, evaporation, and decoction, and may be applied either by direct contact with the burning fuel or through the agency of some interposed medium. The use of coal as a fuel for the production of steam is confined to manufacturing establishments, the retail pharmacist finding illuminating gas or some of the various kinds of coal-oil better adapted to his wants. Wherever illuminating gas is available it is decidedly the most desirable fuel at the present day, not only because its supply is constant, but also because with modern apparatus and appliances it can be kept completely under control, and thus the greatest amount of heating power be obtained at a minimum of cost. In the course of time electricity will no doubt become a serious competitor of gas for heating purposes in pharmaceutical laboratories, as its use in the arts and for domestic purposes has already demonstrated. Fig. 44 illustrates an electric plate-stove, simple in construction and very convenient for boiling and distilling inflammable liquids.

FIG. 44.

Electric plate-stove, showing switch for regulating the current.

Gasoline vapor and kerosene are extensively employed for the generation of heat, in localities where illuminating gas cannot be procured; although both are quite cheap in price, a certain element of danger attends the use of the former, while the latter is open to the objections that it cannot be burned without the aid of a wick, that it deposits soot unless the wick is carefully watched, and that its combustion is frequently accompanied by a more or less disagreeable odor. For small operations alcohol offers an excellent fuel of good heating capacity; its high price forbids its more extensive use.

The *amount of heat* produced by the combustion of any particular fuel is constant, no matter how the combustion is effected; but the *intensity of heat* is dependent upon the rapidity of combustion; therefore, the finer the division of the fuel, the more rapidly will it be burned or oxidized, and consequently the greater will be the degree of heat generated.

Various appliances have been designed for the production of heat for pharmaceutical purposes, of which a few are shown herewith, as it is assumed that either gas or coal-oil is available everywhere.

When the price of alcohol is not an object, this fuel is preferable

to coal-oil where illuminating gas is not available. Fig. 45 represents a very convenient form of spirit lamp, nickel-plated and provided with a regulating screw for the wick; it is not easily upset and answers well for small operations at the dispensing counter.

Fig. 45.

Nickel spirit lamp.

Fig. 46.

Barthel's alcohol lamp.

Barthel's alcohol lamp, Fig. 46, was introduced in Germany in 1891, and is capable of producing an intense heat by the combustion of alcohol vapor. This lamp, which is perfectly safe, is extensively used in Europe; it is made of metal, has a lateral capped orifice for filling, and bears a central tube, closed on top, which carries a solid wick. This is not itself ignited, but only serves to draw up alcohol from the reservoir. To the wick-tube is attached a second tube, the burner-tube proper, which receives the vapors from the wick. The burner-tube contains a wire diaphragm, which can be raised or lowered by means of the regulating screw, and thus a higher or lower flame obtained as desired. When the lamp is to be used, the wick-tube must be heated slightly by means of a lighted match, so as to drive some alcohol vapor into the burner-tube, where it is then ignited. It will then continue to draw up alcohol vapor of its own accord. The efficiency of the lamp is shown by the fact that a quart of water can be raised from 60° F. to the boiling-point in eight and three-quarter minutes, with an expenditure of about one ounce of alcohol; low-grade alcohol of 75 or 80 per cent. evaporates less rapidly than stronger alcohol and produces equally good results.

Fig. 47.

Whitney's coal-oil stove. (Single burner.)

For the combustion of coal oil, stoves are now manufactured which are claimed to produce a smokeless and odorless flame; the heating capacity of these stoves is quite considerable, and is regulated by means of screws for raising and lowering the wick. Fig. 47

represents the Whitney Patent Hot-blast Stove, in which the wick chamber is separate from the oil reservoir. Coal-oil stoves may be had with one, two, or three wicks, and require some attention, so that the wicks shall always be kept well trimmed and free from carbonaceous matter; to avoid a deposit of soot, the wick should never be allowed to touch the vessel to be heated.

It is well known that the illuminating power of gas depends upon the incandescence of particles of unconsumed carbon, and that if these particles be brought to complete combustion by the appropriate use of air (atmospheric oxygen), the luminosity of the flame will be decreased, but its heating power will be intensified. A yellow carbonized flame, also known as oil flame, because resembling that produced by the combustion of oil, is never well adapted for heating purposes, besides

FIG. 48.

Fletcher low-temperature burner.

FIG. 49.

Foot-blower.

depositing considerable soot or carbon on the bottom of vessels placed over it. In all modern gas-heating apparatus, proper provision is made for mixing the illuminating gas with such a proportion of air that, when the mixture is ignited, a purely blue flame will result, indicative of complete combustion; burning alcohol resembles such a flame. A large variety of gas burners and stoves is now offered, intended to furnish both high and low powers of heat. Of these probably none has a wider range in heating capacity than the Fletcher low-temperature burner (Fig. 48), any degree of heat from a gentle current of warm air to clear red heat being obtainable; it is manufactured by the Buffalo Dental Manufacturing Company, of Buffalo, N. Y. The burner consists of a ring of iron tubing, D, perforated on the upper side, and enclosed in a cylinder of cast iron, over which a diaphragm of wire gauze, A, is fastened; there is a space, B, between the lower end of the cylinder and the bottom of the apparatus, for the admission of air, and a tube, C, for the attachment of a pipe from a bellows when a blast is to be used for producing powerful heat. When a gentle heat is desired, the gas is lighted through the opening B, thus heating the air as it flows up-

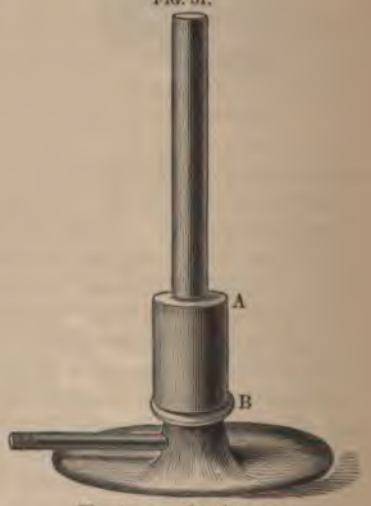
ward and escapes through the gauze A. For a stronger heat the gas and air mixed are lighted above the wire gauze, and a steady, smokeless, blue flame is thus obtained. As any rubber tubing attached to D is apt to become very hot, it should either be wrapped with a small wet cotton cloth, dipping in water, or, what is still better, about eight inches of gas-pipe should be permanently attached to D, to which the rubber supply-tube may be secured when wanted. Fig. 49 represents a convenient foot-blower for use with any gas furnace requiring a strong supply of air; the rubber disk is well protected by netting.

For small operations at the dispensing counter, Bunsen burners are usually employed, which are so constructed that a small supply of gas is made to yield a strong heat by admixture with air, whereby perfect combustion is effected. One drawback to the majority of Bunsen burners in the market is the tendency to "light back"—that is, when the flame is reduced, it is apt to recede and ignite the gas at the pinhole orifice in the tube; the most effectual method of overcoming this difficulty is to contract the orifice of the tube and introduce a gauze diaphragm into it near the top, which, however, reduces the heating power of the flame. Among the large variety of Bunsen burners sold, a few have been found specially adapted to the use of the pharmacist, and are here illustrated. Fig. 50 represents a low form of burner, 3 inches high, made in

FIG. 50.

Bunsen burner, low form with crown.

FIG. 51.



The Acme safety burner.

two sizes, with tubes of $\frac{5}{16}$ and $\frac{5}{8}$ inch in diameter respectively; with the aid of a contracted brass cap, the flame can be turned down quite low without receding. When it is desired to distribute the flame, the brass crown shown in the cut should be attached, after removal of the brass cap; the crown, being provided with three supports, does away with the necessity for a tripod. The burner is made by Bullock & Crenshaw, of Philadelphia, and will be found very

serviceable for all smaller operations. In Fig. 51 is shown the Acme Burner, patented in 1891 by T. Boyce, of New York; this is probably the most satisfactory burner made for small operations at the dispensing counter, and can be used for coal or gasoline gas. Each burner is provided with two tubes, one of the regular Bunsen pattern, the other with a gauze safety-tip (Fig. 52), permitting the flame to be turned down as low as desired, and out without receding. The supply of gas is regulated by turning the tube at A until the desired quantity of flame is obtained; by turning the milled disk, B, up or down, it being threaded and moving upon the nipple, the air-supply is adjusted. The height of the burner is $5\frac{1}{2}$ inches, including the base. The Finkner burner (Fig. 53) yields a very satisfactory flame, but is not adapted for very strong heat; it is so constructed that the supply of gas and admixture of air can be simultaneously regulated by turning the milled head. Fig. 54 represents a convenient adjustable burner; by turning the screw, which is accessible to the fingers while the burner is in use, the gas orifice can be so adjusted that any desired flame may be had. The air-supply is adjusted by turning the air-regulator up or down, it being threaded and moving upon the burner tube. The moving of the point up through the gas orifice, while reducing the gas quantity and size of the flame, does not reduce the gas pressure; the gauze safety-tip

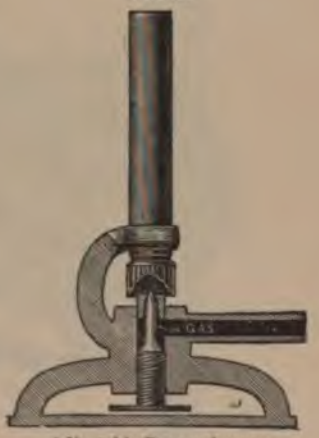
FIG. 52.

Gauze tip and tube for the Acme burner.

FIG. 53.

The Finkner burner.

FIG. 54.



Adjustable Bunsen burner.

(Fig. 52) can also be attached to this burner when a very small flame is desired. For maintaining low temperatures, as in the

testing of pepsin and similar operations, the double minim burner (Fig. 55) will be found useful.

For use with inflammable liquids the apparatus illustrated in Fig. 56 will be found serviceable, the burner being surrounded with safety

FIG. 55.

Double minim burner.

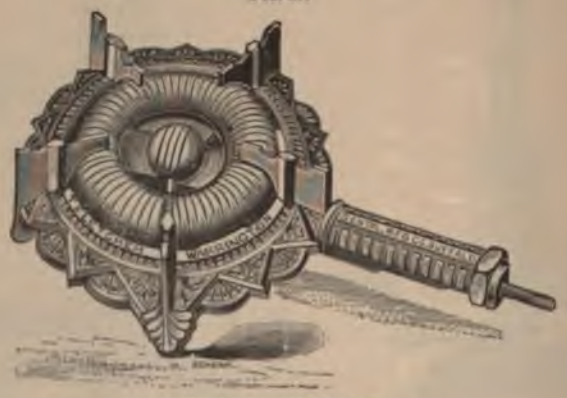
FIG. 56.

Safety burner, to be used for heating inflammable liquids.

gauze, which prevents the flame from communicating with the vapor on the outside, the principle being the same as in the Davy safety lamps.

Fletcher's radial burner (Fig. 57) possesses some advantages over other heaters, in containing no loose parts and in being made entirely of annealed cast-iron; it is practically indestructible; if choked with dirt it is readily cleaned with a card or spatula. The flames are practically *solid* when in use, and show no tendency to run to a point in the centre; the consumption of gas amounts to from 12 to 18 feet per hour, and the burner will accommodate vessels from 10 to 18 inches in diameter.

FIG. 57.



Fletcher's radial burner.

For larger operations the "Jewel" gas-stove, Fig. 58, manufactured by Geo. M. Clark & Co., Chicago, will be found very serviceable. The cast-iron frame is twelve inches square and five inches high, thus standing very firm and capable of supporting large vessels. The gas is properly mixed with air before it enters the radial burner, where perfect combustion is effected, as shown by the pale-blue flame, which can be turned down very low without flickering. It consumes about eight feet of gas per hour, and is a most efficient heater.

FIG. 58.

Jewel gas stove.

For regulating the degree of heat within certain narrow limits, special appliances have been devised, known as thermostats, by means

FIG. 59.

Reichert's thermostat.

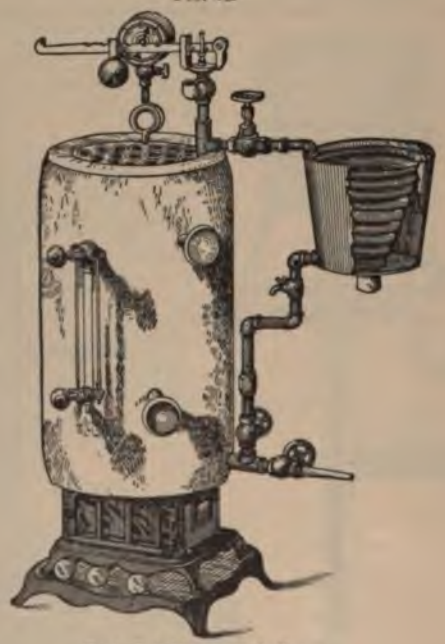
FIG. 60.

The Bunsen-Kemp gas regulator or thermostat.

of which the supply of gas admitted to the burner is automatically controlled by expansion and contraction of mercury contained in glass cups or tubes kept in contact with the air or liquid the temperature of which it is desired to maintain at, or near, certain points. All gas supplied to the burner is made to pass through the thermostat, and the required temperature having been reached, the gauge is set by means of a screw, after which the supply of gas is controlled by the expansion of the mercury caused by an increase of heat. Figs. 59 and 60 show two thermostats frequently employed.

The steam boiler, Fig. 61, designed by Prof. E. L. Patch, is a

FIG. 61.



Prof. Patch's steam boiler.

most convenient source of heat for the requirements of a small laboratory. The boiler, 22 inches high and 10 inches in diameter, is made of steel, contains 20 flues, and is covered with a thick layer of asbestos composition, to prevent loss of heat by radiation; it has a capacity of 7 gallons and possesses one great advantage—that it can be heated by means of either a gas or a coal-oil stove. Being provided with a water-gauge, safety-valve and manometer, the boiler is as complete as any of larger size, and steam can be carried from it to any point desired; it is usually filled from above at the safety-valve, but, wherever water service is available, an injector may be attached, so as to allow of filling while steam pres-

sure is on. The coil of pipe in the conically shaped metal case on the side, may be used for hot filtration, evaporation or drying purposes.

It is well known that steam, when confined, is capable of absorbing large quantities of heat, and its temperature rises proportionally to the pressure exerted upon it; dense aqueous solutions, therefore, can readily be boiled by means of superheated steam.

For the proper control and distribution of heat, different devices are employed. When direct flame is to be applied to porcelain or glass vessels the interposition of wire-gauze or asbestos cloth will be found very desirable; for not only will the heat be supplied to a greater extent of surface by radiation, but at the same time it will

FIG. 62.

Sand-bath, shallow form.

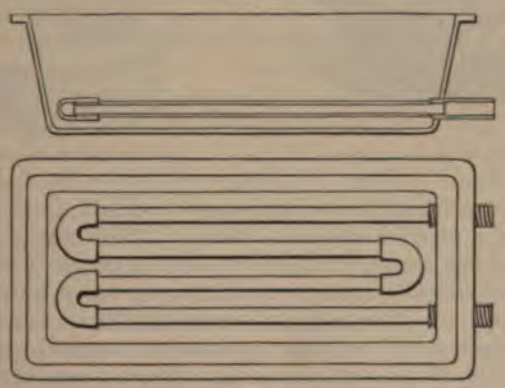
FIG. 63.

Sand-bath, deep form.

be uniformly distributed, and thus insure more regular heating, which of itself is very important, considering the frail character of flasks and dishes.

The sand-bath is employed for temperatures above that of boiling water, and is chiefly intended to maintain a continuous supply of high

FIG. 64.



Large sand-bath, heated by steam.

heat and to prevent sudden depression of temperature from foreign causes; it is invaluable in the distillation of certain liquids (acids, etc.) from glass vessels, and may be either of deep or shallow form. (See

Figs. 62 and 63.) The deep sand-bath consists of an iron pot or basin containing sufficient dry fine sand so that, if desired, the retort or flask may be entirely surrounded by the same. The best shallow sand-baths are made of Russian sheet-iron, and are well adapted for heating flasks and beakers, which require only sufficient sand to form a good bed of support, since an excessive amount would involve a waste of heat.

For use in a laboratory where steam is available, a permanent sand-bath may be provided as shown in Fig. 64. It is constructed from an ordinary galvanized-iron sink and large gas-pipe, about three-quarters to one inch in diameter, arranged horizontally in folds, the ends of the pipe being introduced through holes of appropriate size drilled in the end of the vessel. Sand to the depth of two or three inches may be poured over the pipes, which will form an excellent bed for flasks, dishes, and beakers.

Other apparatus for the use of heat above that of boiling-water, yet avoiding contact with flame direct, are oil-baths, saline solution baths, glycerin baths, or paraffin baths; these are constructed like water-baths, and readily furnish temperatures ranging from 100° to 300° C. (212° to 644° F.).

For all operations requiring a degree of heat below that of boiling-water, water-baths will be found indispensable; they may be made with either a round or flat bottom, as shown in Figs. 65 and 66, and

Fig. 65.

Round-bottom water-bath.

Fig. 66.

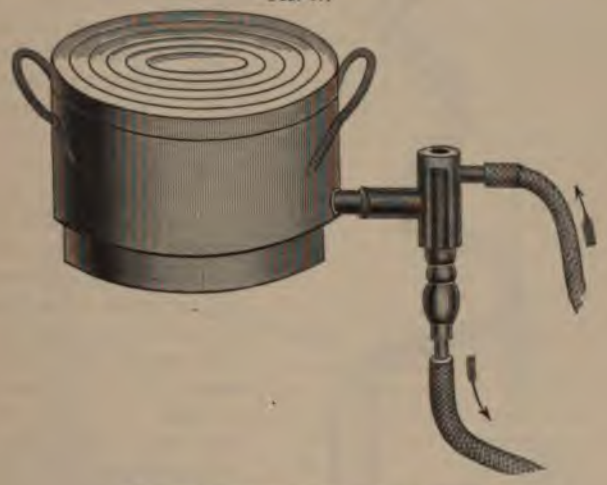
Flat-bottom water-bath.

provided with a set of concentric rings to adapt them for use with dishes or flasks of various sizes. Water-baths made of extra heavy tin will last a long time (provided they be dried properly after use), and do not cost much, while copper is far more expensive, but, on the other hand, resists the action of heat and water better than tinned iron. As long as the vapor of boiling water is allowed to escape freely, no amount of heat applied to the vessel can possibly increase the heat of the water above that of boiling, and, as some heat-power is lost during transmission from the water-bath to the vessel resting upon it, the liquid contained in such vessel will always be found a few degrees lower in heat than the water in the bath; under no circumstances can aqueous liquids be made to boil in dishes placed in water-baths.

The name vapor-bath is in the majority of cases more appropriate than water-bath, since the vessel heated by it does not, as a rule, come in contact with the water for any length of time, but derives its heat from the vapor or steam rising from the water and not confined by pressure.

To avoid frequent refilling and consequent interruption in long-continued operations, water-baths are often provided with a constant supply attachment as shown in Fig. 67, which also serves to keep

Fig. 67.

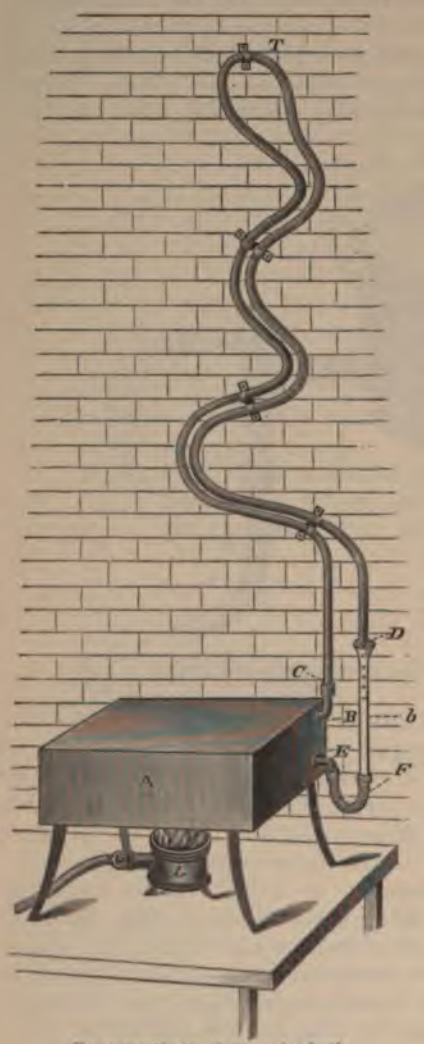


Water-bath with constant-level attachment.

the water at a constant level in the bath. The best contrivance for a constant water-bath is that suggested by Dr. B. F. Davenport, of Boston, and shown in Fig. 68. It consists of a copper box, *A*, 10 or 15 inches square, the top being a brass plate $\frac{1}{8}$ inch thick, to enable it to bear considerable weight without yielding. From the point *B* projects a $\frac{1}{2}$ inch brass tube, *B C*, which turns up at a right angle. At *E* is a stopcock which is connected by a thick rubber tube with the glass tube, *D F*, the latter being fastened against the adjoining wall. Connected with *C* by a rubber tube-joint is a $\frac{1}{2}$ inch block tin tube of 20 feet length, which extends up the wall, to which it is fastened for 10 feet to the point *T*, whence it returns and ends just over the top of the glass tube at *D*. The bath is filled with water (preferably distilled) to just the level, *B*..*b*. The steam generated by the constant boiling is condensed in the tube, *C T D*, either before or after reaching the top, *T*, and returns to the bath at *C* or at *D*, where it drops into the glass water-gauge, *D F*. Having once been filled, the water need not be replenished for years, and there being no outlet for the steam, except into the condensing tube, the air surrounding the water-bath will be kept constantly dry—a very

desirable point in the evaporation of liquids. If the water-bath is desired for use at fixed temperatures a thermometer may be introduced through a cork fitted to a tube inserted in the cover of the bath.

Fig. 68.



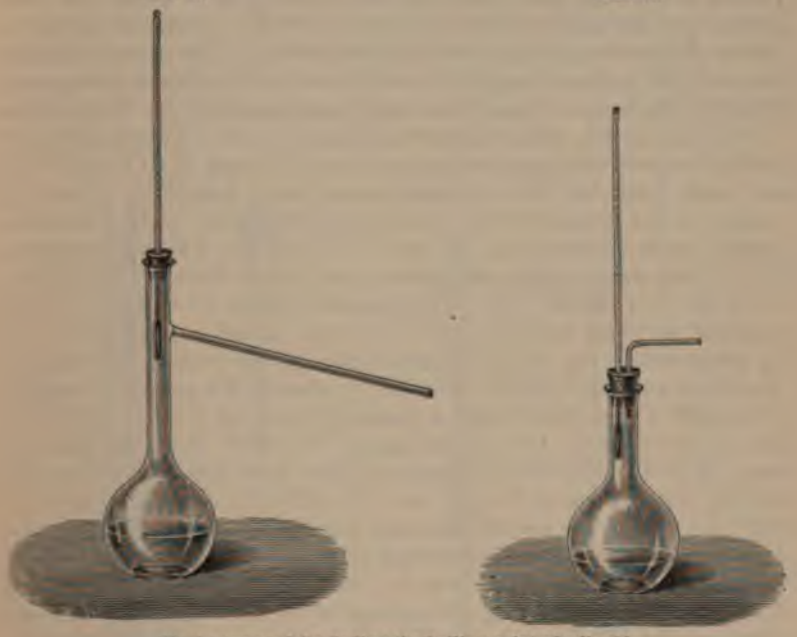
Davenport's constant water-bath.

The boiling-point of a liquid is that at which the elasticity of its vapor overcomes the pressure of the surrounding atmosphere, or, in other words, beyond which the liquid cannot continue as a liquid without increased pressure. Normal atmospheric pressure, 15 pounds to the square inch, which is equal to the pressure of a column of mercury 760 Mm. (29.87+ inches) in height, is always assumed when referring to the boiling-point of a liquid, for any modification of the former will change the latter; thus water, which ordinarily boils at 100° C. (212° F.), has been known to boil at 84° C. (183.2°F.) on Mont Blanc, in Switzerland, and even at 35° C. (95° F.) in a vacuum apparatus; while, under greatly increased pressure, as in Papin's digester, it has been heated to 160° C. (320° F.) without boiling. There exists also a great variability in the boiling-points of different liquids under normal conditions; for, while official ether boils at about 37° C. (98.6° F.), chloroform requires a temperature of 60.5° C. (140.9° F.), alcohol 78° C. (172.4° F.), glycerin 165° C. (329° F.), and mercury about 357° C. (674.6° F.).

The simplest method for determining the boiling-point of a liquid is to introduce some of it into a flask provided with a lateral tube in the neck and a thermometer passing through the cork, as shown in Fig. 69, or into an ordinary Florence flask provided with a doubly-

perforated cork, through one orifice of which a thermometer is inserted and through the other a bent glass tube, as represented in Fig. 70. If inflammable or noxious vapors are likely to be evolved, the tube from either flask may be connected with a condenser. It is important that the thermometer should not be immersed in the liquid, but only introduced into the flask so far that the bulb may be enveloped by

FIG. 69. FIG. 70.



Flasks arranged for finding the boiling-point of a liquid.

the vapor of the boiling liquid, as shown in the illustrations. Heat should be carefully applied and gradually increased until the liquid boils actively, at which time the boiling-point will be indicated by the height of the mercurial column in the thermometer. In the case of very accurate determinations, it may be necessary to make corrections for increased or decreased atmospheric pressure, and according to Kopp the correction amounts to 1° C. (1.8° F.) for every 27 millimeters above or below the normal height of the barometer column of mercury. In order to avoid errors, which might arise from the cooling of the long mercurial column outside of the flask, specially constructed thermometers, known as Zincke's thermometers (see page 90) are usually employed for temperatures above 100° C. (212° F.).

Fusible substances, when gradually heated to their melting-point, do not all behave in the same manner; as a general rule, crystallizable bodies become brittle just before melting, while non-crystallizable substances assume a plastic condition. When fusion commences they

combine, as it were, with heat in an intimate manner; that is, they occlude heat, so that the further addition of heat does not cause any rise in temperature until all of the substance has become liquefied. The heat thus disappearing is called the latent heat of fluidity, because it is used to change the solid form of a body into the liquid form without any change in the temperature of the body; thus if crushed ice be heated, the temperature will not vary from 0° C. (32° F.) while the ice is melting, and when completely changed to water, the temperature of the water will also be 0° C. (32° F.), provided the application of heat be not continued beyond fusion. The amount of heat necessary to produce complete fusion varies with different substances; thus in the case of ice it has been ascertained to be 79.25 C. or 142.65 F. degrees; this was determined as follows: Two vessels, containing respectively equal weights of ice and water at 0° C. (32° F.), and each provided with a thermometer, were heated in a bath of water; at the moment when the ice had completely melted the temperature was indicated as still at 0° C. (32° F.), while the temperature of the water in the other vessel had risen from 0° C. (32° F.) to 79.25° C. (142.65° F.). If a pound of ice at 0° C. (32° F.) and a pound of water at 100° C. (212° F.) be mixed so as to avoid loss by evaporation, the result, when all the ice has melted, will be two pounds of water at 10.4° C. (50.7° F.); whereas if a pound of water at 0° C. (32° F.) be mixed with a pound of water at 100° C. (212° F.), the result would be two pounds at 50° C. (122° F.). In the first case, 79.25 C. (142.65 F.) degrees of heat were withdrawn from the boiling water to melt the ice at 0° C. (32° F.) into water at 0° C. (32° F.), but in the second case this was not necessary, and the mixture assumed the mean temperature of the two. The latent heat of fluidity of water being known as 79.25° C., a simple rule can be formulated for ascertaining the amount of ice necessary to reduce any given weight of water at stated temperature to a stated lower temperature, as follows:

Add the desired temperature to 79.25° C. (142.65° F.) and divide the sum into the difference between the stated temperature of the water and the desired temperature—the quotient will be the required proportion of ice as compared with the given weight of water.

Example: How much ice is required to cool 1000 Gm. of water from 100° C. to 25° C.?

```
 79.25        100.0        104.25 )  75.000  (0.7194
 25.00         25.0                   72975
 ------       ------                 ------
 104.25        75.0                   20250
                                      10425
                                     ------
                                      98250
                                      93825
                                     ------
                                      44250
                                      41700
                                     ------
```

Answer: 0.7194 of 1000, or 719.4 Gm.

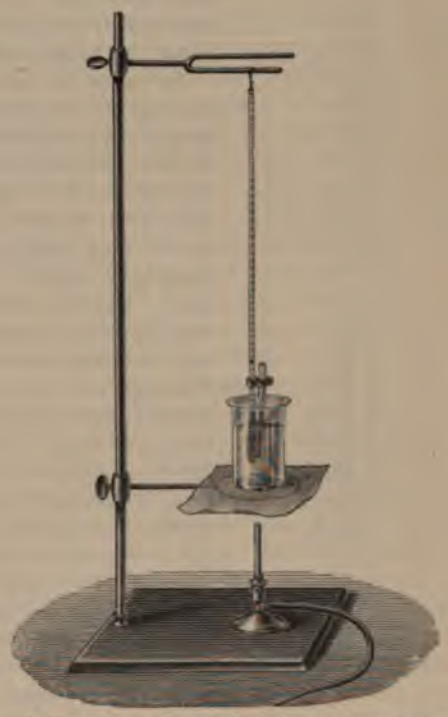
Proof: The ice needs 25° C., besides the 79.25° C. required for melting it, and the water loses 75° C. by being reduced to 25° C.; as the gain and loss must balance each other, it will require $\frac{75}{104.25}$ of 1000 Gm. of ice, or 791.4 Gm.

The law regarding latent heat of fluidity has a practical bearing upon the fusion of various substances liable to be injured by exposure to a heat a little above their melting-points; thus, a pan of ointment or plaster may be kept over a direct fire, without fear of injury, *as long as a portion of the contents remains unmelted*, as the increased amount of heat is utilized in the change of the state of aggregation, therefore it cannot raise the temperature above that of the melting-point.

FIG. 71.

Capillary tube and thermometer with tube attached.

FIG. 72.

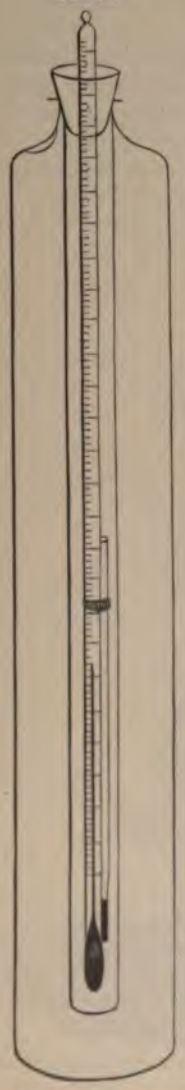


Ordinary method of finding the melting-point of substances.

The melting-points of solids are as variable as the boiling-points of liquids; thus, while ice melts at 0° C. (32° F.) and lard at 39° C. (102.2° F.), sulphur requires a temperature of 115° C. (239° F.) and pure morphine a temperature of 255° C. (491° F.)

The determination of the melting-point of a substance frequently leads to its identification, and is a most valuable adjunct in the examination of its quality. Some little care is requisite in determining the melting-point so as to insure accurate results. The best plan is to put a little of the substance to be examined into a small capillary tube (Fig. 71), and, after cutting off the enlarged portion, which is only intended for convenience in filling, attach the tube to an accurate thermometer by means of a rubber band, in such a manner that the tube lies close against the thermometer and the substance is on a line with the bulb, as shown in Fig. 71. The thermometer thus arranged may be suspended in a beaker containing water, sulphuric acid, or paraffin, as shown in Fig. 72. The liquid is gradually heated and the temperature accurately noted when the substance in the capillary tube melts.

Fig. 73.



Improved apparatus for the determination of melting-points.

In order to insure greater uniformity in the heating of the mercurial column of the thermometer, a very excellent apparatus has been devised by Dr. Alfred Dohme, of this city, the construction of which is very simple and is shown in Fig. 73. Into the neck of a rounded glass cylinder 9 inches long and 1½ inches in diameter is fused a glass tube closed at one end and ½ inch in diameter. The thermometer, to which is attached the capillary tube containing the substance, is inserted into the inner tube by means of a perforated cork. Through the opening in the shoulder sulphuric acid is poured into the outer cylinder to the height of about 7½ inches, and the apparatus having been supported by means of a burette clamp, heat is carefully applied, and the currents thus established in the acid communicate heat to the air in the inner tube, which is kept uniform by circulation of the fluid. As in the preceding experiment, the melting-point is noted by the height of the mercurial column when the substance melts.

The term *temperature* is used to designate *intensity* but not *quantity* of heat, which is measured by a thermometer, an instrument consisting of a narrow capillary tube of uniform bore, hermetically sealed at the upper end, and terminating below in a bulb of glass. The bulb and a portion of the tube are filled with mercury (in some cases with colored alcohol or toluene), and the whole is provided with a graduated

scale for measuring the rise and fall of the liquid within the tube; mercury is preferred for all temperatures not below —40° C. (at which point it freezes), on account of its non-adhesion to the sides of the glass tube, and consequent convex surface, and its great sensitiveness to even the slightest change in temperature. Absolute alcohol, although admirably adapted to very low temperatures, cannot be used for measuring heat intensity above 78.3° C., its boiling-point. The space above the liquid in the tube is deprived of air, so as to insure the ready and uniform rise of the liquid when expanded by heat.

As all glass vessels continue to contract for some years after they have been made, absolutely correct measurement of temperatures can only be obtained if the error of the thermometer is known; such error can easily be ascertained by two very simple experiments. Immerse the bulb of the thermometer in crushed ice for fifteen or twenty minutes, and note the point on the graduated scale to which the mercury will sink; after five minutes more of immersion, again examine to see whether the mercury has remained stationary; if the mercury receded to 0° C. (32° F.) and remained at this point, the thermometer is correct as far as the freezing-point is concerned. To test its accuracy at higher temperatures, suspend the thermometer in steam rising from pure boiling water, in such a manner that it is completely surrounded by it, for the unconfined vapor of a boiling liquid has the same temperature as the boiling liquid itself; after thirty minutes, note the point to which the mercury has risen and continue the heat for ten or fifteen minutes, and examine again; if the mercury has risen to 100° C. (212° F.) and remained at that point for ten or fifteen minutes, the thermometer may be considered correct as compared with the boiling-point of water. Clinical thermometers, used by physicians for taking the temperature of fever patients, should be supplied with a certificate showing their error, as this in some cases may amount to nearly ½ degree. Since 1880 the Winchester Observatory at Yale College, New Haven, Conn., has had in operation a special bureau for the examination of thermometers; as glass tubing will continue to contract for three or four years, clinical thermometers should have been "seasoned" for at least that time before they are examined, so that any error found may remain constant.

During the past two years, thermometers of great accuracy, intended for very high temperatures, up to 550° C. (1022° F.), have been made in Germany, of special glass, known as "Jena resistance glass," which is very hard and non-contractile. In order to prevent boiling of the mercury, which ordinarily occurs at about 357° C. (674.6° F.), the capillary tube is expanded at the upper end and filled above the mercurial column with compressed dry carbon dioxide. Still more recently (1894) thermometers have been manufactured in which the indicator consists of an alloy of sodium and potassium, instead of mercury, and which may be used for temperatures running as high as 650° C. (1202° F.). The alloy is enclosed,

as in the previous case, in "resistance" glass, and the space above the alloy is filled with nitrogen at such pressure that, when the bulb becomes red-hot, the pressure inside is equal to that of the atmosphere. The glass of the bulb is attacked by the alloy and turned brown, but this occurs at the time of filling, and the coating then formed upon the surface of the glass protects it from further action.

For registering still higher temperatures, instruments known as pyrometers are employed, which are, however, not very trustworthy; they are of two kinds, Wedgewood's pyrometer, based on the contraction of clay, and Brogniart's pyrometer, based on the expansion of metals. When it is desirable to note the highest or lowest temperature reached during any fixed time, maximum and minimum thermometers, so constructed that a small metallic or glass indicator is carried to the highest or lowest point reached by the mercury or alcohol, and left at that point when the volume again changes, are used.

Three different thermometric registers, known as the Fahrenheit, Celsius or Centigrade, and Réaumur scales, are in use. For scientific purposes the Centigrade scale is now universally employed, while the Fahrenheit scale is in common use in this country and Great Britain, and the Réaumur scale is ordinarily used in Continental Europe. The graduations of all three scales are arbitrary, yet based upon careful observations of the respective authors. Fahrenheit, a German, who invented the mercurial thermometer, in 1709, observed that a quantity of mercury immersed in a mixture of ice and salt (considered by him as the absolute zero of temperature) amounted to 11,124 volume parts, and when immersed in melting ice expanded to 11,156 volume parts, showing an increase of 32; the same quantity of mercury immersed in boiling water expanded to 11,336 volume parts, or an increase of 212.

These observations led Fahrenheit to mark the freezing and boiling points of water at 32 and 212 degrees above zero respectively, and to divide the space between these two points into 180 equal parts. Réaumur, a Frenchman, found that 1000 volume parts of alcohol of a given strength increased to 1080 volume parts between the freezing and boiling points of water, and he marked these two extremes as 0 and 80 respectively, dividing the intervening space into 80 equal parts. Celsius, a Swede, adopted the more convenient plan of centesimal division, and fixed the freezing and boiling points of pure water at 0 and 100 respectively; his scale is generally termed the Centigrade scale and is preferred for scientific work.

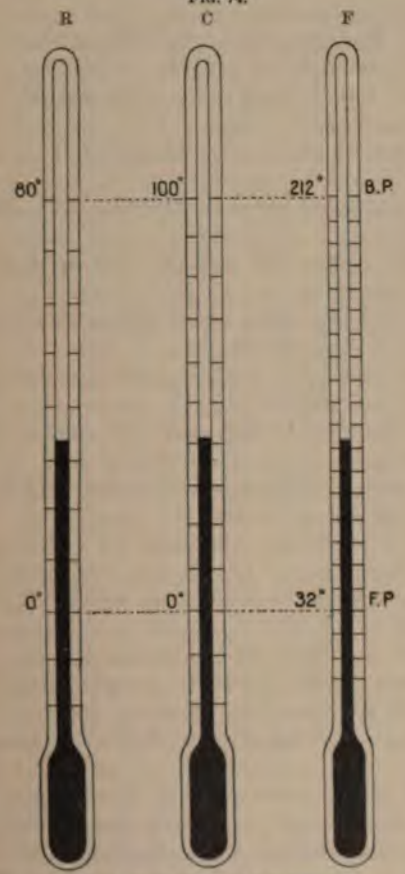
When writing temperatures on the different scales, it is customary to use the abbreviations F. or Fahr. for Fahrenheit, C., Cent. or Cels. for Celsius, and R. or Réaum. for Réaumur, as, 32° F., 100° C., and 80° R. On all the scales, the degrees are divided into *plus* and *minus* degrees, as they may be above or below the zero point; the latter being always distinguished by the prefix of the — sign, and whenever this sign is wanting, the degrees of heat being understood to be above

zero; thus 18° F. would indicate 18 degrees above 0, although 14 degrees below the freezing-point, etc.

Fig. 74 illustrates the relative graduations on the respective thermometric scales.

As equal spaces on the Centigrade and Fahrenheit scales are divided into 100 and 180 degrees respectively, it follows that each degree on the former scale is equal to 1.8 degrees on the latter, and since 80 degrees on the Réaumur scale equal 180 degrees on the Fahrenheit scale, every degree of the former must correspond to 2.25 degrees of

Fig. 74.



Réaumur, Centigrade, and Fahrenheit thermometers.

Fig. 75.

Section of Zincke's thermometer.

the latter. Every Réaumur degree is equal to 1.25 Centigrade degrees. The following rules for the conversion of thermometric values are useful.

To convert Centigrade into Fahrenheit: *Multiply by* 1.8 *and add*

32; for any number of degrees above or below the freezing-point on the Centigrade scale when multiplied by 1.8 yield the corresponding number of degrees above or below the freezing-point on the Fahrenheit scale.

To convert Fahrenheit into Centigrade: *Subtract* 32 *and divide by* 1.8; for any number of degrees above or below the freezing-point on the Fahrenheit scale when divided by 1.8 yield the corresponding number of degrees above or below the freezing-point on the Centigrade scale.

To convert Réaumur into Fahrenheit, or Fahrenheit into Réaumur, *substitute* 2.25 *for* 1.8 *in the preceding rules.*

To convert Centigrade into Réaumur, *divide by* 1.25; and to convert Réaumur into Centigrade, *multiply by* 1.25.

Examples: Convert 25° C. into F.; $25 \times 1.8 = 45$ and $45 + 32 = 77$. Answer, 77° F.

Convert —15° C. into F.; $-15 \times 1.8 = -27$ and $-27 + 32 = 5$. Answer, 5° F.

Convert —40° C. into F.; $-40 \times 1.8 = -72$ and $-72 + 32 = -40$. Answer, —40° F.

Convert 60° F. into C.; $60 - 32 = 28$ and $28 \div 1.8 = 15.55+$. Answer, 15.55+° C.

Convert 18° F. into C.; $18 - 32 = -14$ and $-14 \div 1.8 = -7.77+$. Answer, —7.77+° C.

Convert —12.5° F. into C.; $-12.5 - 32 = -44.5$ and $-44.5 \div 1.8 = -24.72+$. Answer, —24.72+° C.

Convert 30° R. into F.; $30 \times 2.25 = 67.5$ and $67.5 + 32 = 99.5$. Answer, 99.5° F.

Convert —5° R. into F.; $-5 \times 2.25 = -11.25$ and $-11.25 + 32 = 20.75$. Answer, 20.75° F.

Convert 50° F. into R.; $50 - 32 = 18$ and $18 \div 2.25 = 8$. Answer, 8° R.

Convert 4° F. into R.; $4 - 32 = -28$ and $-28 \div 2.25 = -12.4$. Answer, —12.4° R.

Convert 60° C. into R.; $60 \div 1.25 = 48$. Answer, 48° R.

Convert —8° C. into R.; $-8 \div 1.25 = -6.4$. Answer, —6.4° R.

Convert 28° R. into C.; $28 \times 1.25 = 35$. Answer, 35° C.

Convert —7.5° R. into C.; $-7.5 \times 1.25 = -9.37+$. Answer, —9.37+° C.

In order to avoid the use of the ordinary long thermometer for temperatures above 100° C., which might frequently prove annoying and give rise to inaccuracies in scientific work, special short thermometers have been devised, so constructed that the graduations of the scale begin a little below the boiling-point of water. (See Fig. 75.) These instruments, known as Zincke's thermometers, are from 4 to 6 inches in length, very accurately made, and are admirably adapted for testing the melting or boiling-point of substances at temperatures above 100° C.

CHAPTER V.

COLLECTION AND PRESERVATION OF CRUDE DRUGS.

ALTHOUGH the collection and preparation of vegetable drugs is not in the hands of the pharmacist, but is carried on, often in a small way, by special drug-gatherers and collectors, it is thought fit to refer to the subject here.

The various parts of plants used in medicine cannot be gathered indifferently at all seasons of the year, since the peculiar juices of the plant in which its activity resides are more abundant in some parts than others at certain periods of the plant's growth. Roots of *annual* plants should be gathered immediately before the time of flowering; those of *biennials*, either late in the fall of the first year, or early in the spring of the second year, after the first appearance of the plant above ground; perennial roots should not be gathered until after two or three years' growth, and, in some cases, even four or five years are allowed for full maturity. Fleshy roots must be sliced, either transversely or longitudinally, previous to drying, in order to expose a larger surface to the air; whilst smaller and fibrous roots do not require this treatment. When artificial heat is to be used in drying roots, a temperature of 50° to 55° C. (about 122° to 131° F.) will be found sufficient, except in the case of a few succulent roots, where the temperature may be raised to 65.5° C. (150° F.).

Barks of trees should be gathered in the spring, but those of shrubs in the autumn, for at these seasons they are most readily separated from the wood. Only the inner bark being employed, the outer epidermis should be removed.

Leaves begin to lose their activity after the flowers appear, for the juices of the plant then go toward nourishing the latter; they should therefore be collected when fully developed, before they begin to wither. Leaves of biennials must be collected during the second season.

Herbs are generally understood to mean the whole plant, although the root is frequently rejected; they should be gathered when in flower. If the flowers are not to be used with the stem, the latter should be collected before the flowers appear, but after foliation.

Flowers are preferably gathered before they are perfectly developed (expanded), since odor and color are then more pronounced; the red or French rose offers a striking example. They should be collected in the morning, after the dew has disappeared, and be dried, without artificial heat, in the shade.

Fruits should be gathered before they are quite ripe; but seeds, the least perishable of vegetable productions, must be perfectly ripe, and require very little drying.

Crude vegetable drugs are rarely deprived of all their inherent moisture by the drug-gatherers, and invariably reabsorb moisture when exposed to a damp atmosphere; before such drugs can be mechanically subdivided they frequently require a further drying by artificial heat, which is effected by spreading the material loosely on shelves in ventilated apartments heated by steam. While drugs containing volatile constituents, such as buchu, valerian, myrrh, spices, etc., demand a moderate heat, others again can be strongly heated until they become brittle, as, for instance, squill; a temperature kept at or below 45° C. (113° F.) will not prove injurious in any case.

The amount of moisture present in freshly gathered botanical drugs varies considerably, ranging from 15 or 20 per cent. in barks and wood to as much as 80 per cent. or more in some roots and leaves, and the object of thorough drying is partly to reduce the bulk, but chiefly to preserve the drug for future use; for if vegetable drugs be packed away in a moist condition they soon begin to mould, or become heated, and undergo rapid deterioration. The loss in weight experienced by thorough drying of drugs is in many cases more than compensated for by the increase in value of the dried article, as in opium and other alkaloidal or resinous drugs. If opium containing 10 per cent. of morphine and 25 per cent. of moisture be dried perfectly, the loss in weight will amount to one-fourth, but the relative proportion of active principle is increased one-third; jalap tubers containing 8 per cent. of resin and 34 per cent. of moisture will lose upon drying about one-third of their weight, but the proportion of resin present is increased 50 per cent. Dried botanical drugs are best preserved in cool, dry rooms in containers which shall exclude sunlight, but permit of free circulation of air; odorous drugs should always be kept separate in order to avoid contamination of others; for instance, a bale of buchu, valerian, or sassafras should never be stored by the side of senna leaves, elm bark, or flaxseed.

As crude drugs reach the pharmacist they are frequently not in a condition to be offered for sale, or to be used in the preparation of medicines, on account of impurities present, and the process of garbling is a very necessary operation. The object of garbling, or picking, is to remove, besides impurities and adulterations, decayed and deteriorated portions of the drug, which not only mar the appearance but are apt to contaminate the still healthy portion, and soon render the whole worthless. Senna leaves are generally accompanied by a considerable proportion of stems, broken capsules, and dust, not to speak of the fraudulent admixtures of stones, shells, etc., made by the gatherer or exporter for the purpose of increasing the weight; as much as 15 per cent. of impurities has been taken from

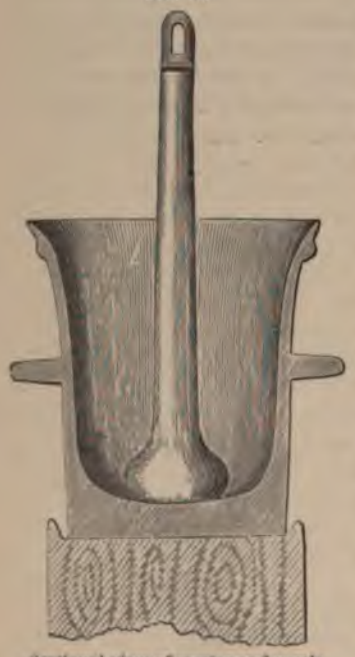
what was bought as prime senna. Juniper berries are never free from unripe and decayed fruit, dirt and worm-eaten portions, which should be carefully removed. Fibrous roots, as spigelia, wild ginger, serpentaria, and the like, require to be freed from adhering dirt and other roots that grow side by side with them, and have become mixed through careless gathering. Although some drugs are found in much better condition than others, there are none which may not be improved in appearance, even if it be only to have the fine dust and dirt removed, as in the case of sassafras, wild cherry, crushed oak-bark, etc.; lycopodium, fennel, flaxseed, and similar drugs, should be well shaken in a suitable sieve, to remove foreign matter, before putting them away in containers, and the careful pharmacist will find that this little extra labor is readily appreciated by his patrons, who are apt to judge a man largely by the appearance of his wares. Even vegetable powders, such as ipecacuanha, nutgall, and others of similar character, must be passed through a fine sieve, preferably bolting-cloth, to remove coarse particles which unfit them for dispensing purposes, and which have, in some instances, been found to amount to as much as 25 per cent. of the total weight of the powdered drug.

CHAPTER VI.

MECHANICAL SUBDIVISION OF DRUGS.

BEFORE employing vegetable drugs in the various pharmaceutical preparations it often becomes necessary to reduce them to a state of comminution, or of powder, more or less coarse or fine as the nature of the drug and the desired preparation may demand. By simple contusion is generally understood a rather coarse division, brought about by crushing or bruising in suitable apparatus preparatory to finer reduction; for small operations an iron or brass mortar of bell or urn shape is employed, which should be deep and with a broad inner base, as shown in Fig. 76, the pestle being of such length and weight as will enable the operator to exercise considerable force if necessary. In contusing substances only such a quantity should be placed in the mortar at one time as to cover the bottom for the depth of an inch or two, and to avoid loss or unpleasant results from the escape of dust or particles of drug, a cover, provided with a hole through which the pestle passes, should be used. In place of the mortar and pestle a cutting knife can frequently be used with advantage. The Champion Knife No. 2, Fig. 77, made by the Enterprise Manufacturing Co., of Philadelphia, is well adapted for the coarse division of roots, barks, and herbs, as it combines a drawing motion with pressure while cutting the material. When operating on large quantities, steam power is necessary, and the best apparatus for the purpose is that known as Mead's Disintegrator (see Figs. 78, 79, and 80). The grinding is done in this mill by hardened steel beaters securely riveted on both sides of a steel disk. These beaters revolve on the feeding side of the mill between corrugated rings. The beaters catch the material as it enters the mill and beat it against the corrugates until it is fine enough to pass between the

FIG. 76.



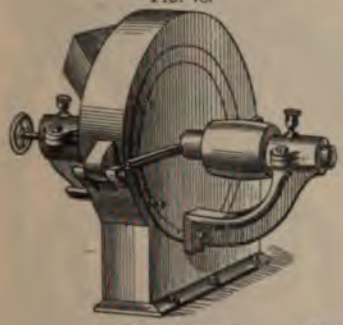
Sectional view of mortar and pestle for contusion.

disk and the face of the ring; as soon as it passes here it is on the discharge side of the mill, and all that is fine enough is immediately

FIG. 77.

Cutter for herbs and roots.

FIG. 78.



Front view.

FIG. 79.

Side view.

Mead's Disintegrator.

driven out by the beaters on the back of the disk. What is not fine enough to discharge is caught by these back beaters and beaten against the screens until fine enough to pass through. The screens are made of square steel, and present a grinding surface to the beaters and a discharging surface between each bar; they are two inches in width and extend around three-fourths of the diameter of the mill, thus giving a large discharging surface without diminishing the grinding surface. The material, as it is ground, falls into the box or room below. The most effective work is achieved with the disintegrator running at high speed, three thousand revolutions per minute; under such conditions, six hundred pounds of wild cherry bark can be finely crushed in an hour.

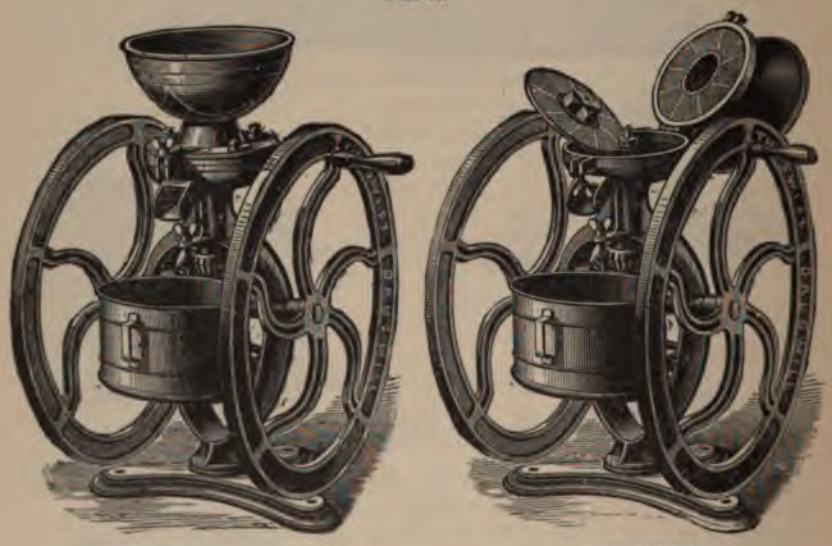
FIG. 80.

a. Section of steel screen; b. Section of corrugated ring; c. Steel disk with beaters attached.

The production of very fine powders of drugs has long since passed into the hands

of the drug-miller, and even the coarser powders intended for percolation are to-day prepared by only a small number of pharmacists. For the latter purpose the drug mills shown in Figs. 81 and 82 will be found very desirable In the New B Swift Mill the grinding is done between plates placed horizontally, while in the Enterprise Mill they are placed vertically. The grinding surfaces of both mills consist of circular chilled-iron castings studded with concentric rows of sharp teeth, those of one plate fitting between those of the other. The teeth decrease in size toward

FIG. 81.



The mill ready for use. The mill open.

New B Swift Mill.

the centre, and the fineness of powder is regulated by a pair of screws, by means of which the plates are made to approximate each other. One of the plates is stationary while the other revolves. Separate sets of plates for coarse and for very fine grinding can be had for the mills. Care should be taken to thoroughly clean the mill after each operation, else the remaining dust will surely contaminate the drug next ground. The simplest method of cleaning is to run sawdust through the mill repeatedly, then loosen the screws and remove the grinding plates, so as to wash these with hot water, if necessary, and dry quickly. A great mistake often made by the inexperienced is the attempt to produce fine powders at once by screwing the plates close together, instead of grinding the drug coarsely at first and gradually tightening the mill; the first plan is apt to cause the material to become heated and cake, while the second plan will achieve the desired end more perfectly, with far less

expenditure of manual labor and wear of machinery. Fig. 83 represents the well-known Hance drug mill, having conical grinding

FIG. 82.

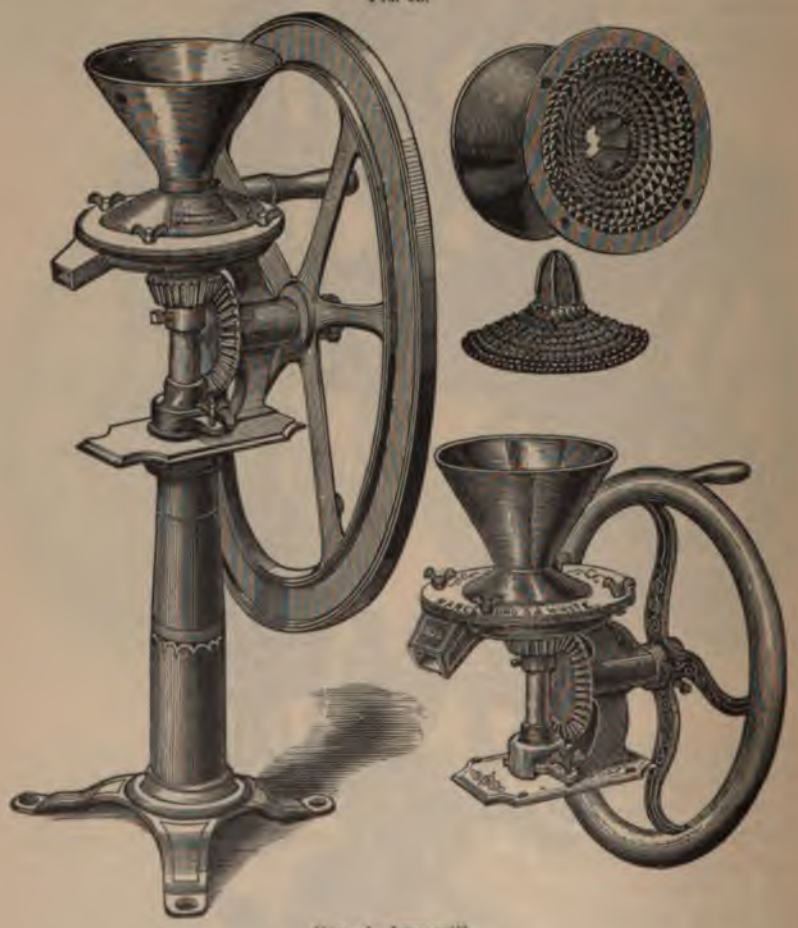
Enterprise drug mill (closed).

Enterprise drug mill (open).

plates, which possess the advantage over the usual styles of not allowing any material to pass through the mill unground (this some-

times happens with vertical plates), and of not holding any of the ground material too long, whereby clogging may sometimes be caused with the horizontal plates. The mill is provided with an iron support, or may be had without it, to be mounted on a heavy block or box. For grinding small quantities at the dispensing counter the No. 450

Fig. 83.



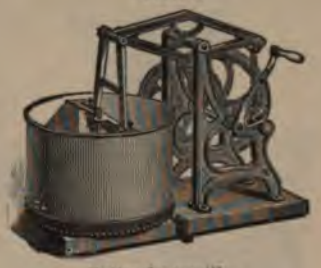
Hance's drug mill.

Enterprise Mill (Fig. 84) is admirably adapted; it is constructed on the same principle as the larger Enterprise Mill shown before. All the before-mentioned hand-mills can be opened horizontally, as shown in the cuts, by means of a thumb-screw and hinge; thus the interior may be readily exposed to view for examination or cleaning. The material is supplied through a capacious hopper, with its base specially arranged for crushing the drug into coarse particles. The

rapidity with which the material should be fed to the mill depends entirely upon the character of the drug, as some drugs will soften under the influence of heat and pressure, while others are not affected at all. Substances like vanilla, which cannot be heated before powdering, on account of the rapid loss of the aromatic principle, must be reduced in the soft condition; and, although the old method

FIG. 84.

FIG. 85.



Cutter for vanilla.

of grinding with sugar or clean sand is still largely in use, it is decidedly inferior to the process of cutting. Grinding or powdering vanilla has a tendency to press out the soft pulp, which soon retards the reduction of the tough fibre and requires the expenditure of much time and labor. If vanilla be reduced to the requisite degree of fineness for percolation by means of a rapid-acting cutter it retains practically its original condition, no pulp being expressed, and a powder is obtained far superior to that by grinding with sand or sugar. Fig. 85 represents the American mince-meat chopper, an apparatus admirably adapted to the cutting of vanilla, and first suggested for this purpose, I believe, by Mr. N. H. Jennings, of this city. The large knife-blade with which the cutting is effected must be kept well sharpened. As the cylinder revolves with each turn of the lever, fresh particles of the material are continually presented to the knife, and disintegration is rapidly achieved, while the aroma and virtue of the vanilla are kept intact.

The grinding of drugs on a large scale, and particularly into very fine powder, is accomplished either in buhr-stone mills, iron mills, such as the Bogardus Eccentric Mill, or stone "chaser" mills. In the first-named mill, grinding is effected between two large stone disks placed horizontally and provided with numerous furrows to facilitate the passage of the ground drug from the centre to the circumference; one of the disks is stationary—in some mills the upper, and

in others the lower—while the other revolves, the material being fed through an opening in the centre of the upper stone. By suitable approximation of the stone disks, powders of various degrees of fineness can be produced.

The portable Bogardus Eccentric Mill (Fig. 86) is a great favorite with drug-millers, as it can be driven at a high rate of speed without becoming heated, and discharges the ground material promptly without danger of choking. Both grinding plates revolve in the same direction, on centres which are about one or two inches apart from each other, hence the name *eccentric;* this arrangement causes the material between the plates to be moved about in every conceivable manner, to be acted upon by the plates at every point, and subjected to a peculiar twisting, cutting, and grinding motion, whereby it is rapidly disintegrated, with large results in quantity ground and the expenditure of but little power. In mills with single revolving plates (the other being stationary), one plate continually describes the same circle on the other, so that material ground in these mills is subject to motion in one direction only, hence greater power and more time are necessary to accomplish the desired result than if the material were acted upon in various directions and by different motions. The rate of feeding the mill is controlled by an adjustable slide attached to the hopper, and the degree of fineness of powder is regulated by means of a screw and lever controlled by a weight.

FIG. 86.

Bogardus eccentric mill.

The so-called Chaser Mill is preferred when large quantities of material, such as cinnamon, ginger, pepper, mustard-seed, and the like, are to be reduced to impalpable powder. Fig. 87 shows a sectional view of a large chaser mill in use at the drug mills of Messrs. Gilpin, Langdon & Co., of this city. It consists of two large stone disks, or granite wheels, connected by a short metallic axle with a revolving shaft, which compels them to travel in fixed lines on a base of granite. The name *chaser mill* is derived from the motion of the disks—called *chasers*—which appear to chase each other in their travels over the stone base. The grinding of any material supplied to the mill is effected between the granite base and the outer edge of the chasers; by means of iron scrapers appropriately fastened to the revolving shaft, the material is continually brought under the grinding edges again. As seen in the illustration, the base is surrounded

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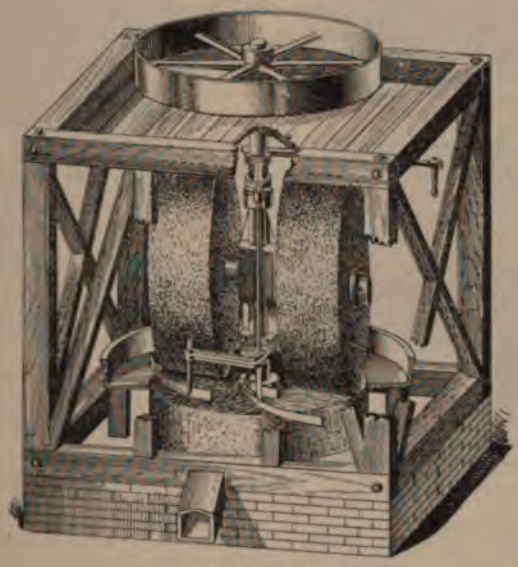
by a curb, to prevent the coarsely-ground particles from mixing with the finer powder, which, by means of the draught created by the rapid revolution of the chasers, is carried upward and over the sides of the curb. The whole mill is enclosed in a dust-proof compartment, which is frequently provided with a series of shelves for the purpose of allowing the fine particles of powder to be deposited for subsequent convenient collection. The feeding of the mill is accomplished through the top of the box, by means of a long funnel delivering the material directly upon the stone base.

FIG. 87.

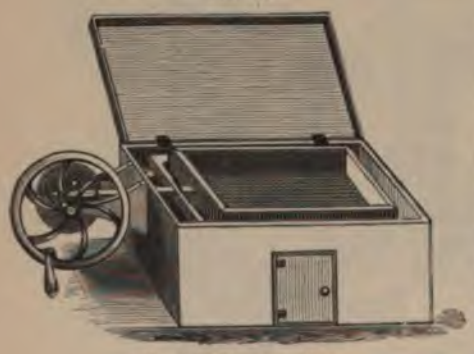


Chaser mill.

SIFTING. In order to produce powder ot uniform fineness, the ground substance should be subjected to the separating action of some perforated medium, whereby division into coarser and finer particles is readily effected. The construction of ordinary sieves is too well known to require special description. The perforated material or netting used may be made of iron, brass, or tinned wire, hair-cloth for substances affected by metal, and silken cloth for very fine or dusted powders. Different degrees of fineness of powder are designated in the U. S. Pharmacopœia by numbers, which refer to the number of meshes to the linear inch in the material of which the sieve is made; thus, *very fine* or No. 80 powder should pass through a sieve having 80 meshes to the linear inch (or 30 meshes to the centimeter); *fine* or No. 60 powder should pass through a sieve having 60 meshes to the linear inch (or 24 meshes to the centimeter); *moderately fine* or No. 50 powder should

pass through a sieve having 50 meshes to the linear inch (or 20 meshes to the centimeter); *moderately coarse* or No. 40 powder should pass through a sieve having 40 meshes to the linear inch (or 16 meshes to the centimeter); *coarse* or No. 20 powder should pass through a sieve having 20 meshes to the linear inch (or 8 meshes to the centimeter). While it is impossible to grind drugs entirely of the degree of fineness wanted for many purposes, the aim should be to keep the finer portion down to a low percentage by frequent sifting; as prescribed in the Pharmacopœia, not more than one-fourth of the powder should pass through a sieve having 10 more meshes to the linear inch. It should also be borne in mind that some parts of the drug can be ground more readily than others; it is therefore necessary to mix the powder thoroughly, after the grinding and sifting have been completed. The proper handling of a sieve cannot be definitely described, it must be taught practically; this much, however, can be said —that no effort should be made to force the material through the meshes of the sieve by persistent pressure of the hand, which will cause the meshes to open farther and allow coarser particles to pass through. In Fig. 88 is shown the well-known Harris Sifting Machine, which some twenty-five years ago was extensively used by pharmacists; its construction is very simple and readily understood. Of late years, sifters and mixers combined in one piece of apparatus have been greatly preferred; such a combination, admirably adapted to the wants of the pharmacist who manufactures on a small scale, is shown in Fig. 89. Its capacity is 50 pounds, and the mixer is provided with a galvanized double spiral agitator so arranged that when the sifted powders come in contact with it the inside spiral carries the material one way, while the outside spiral carries it the other; thus a most thorough mixture is effected in a short time. After the powders have been mixed, the contents may be withdrawn by means of a slide in the bottom of the circular mixer. Smaller and larger sizes of the Lightning Sifter and Mixer are manufactured, and can be supplied with sieves of different degrees of fineness. Fig. 90 represents Jones' Mixer and Sifter, in which the mixing is effected on a different principle, by means of paddles and brushes; its capacity is 10 pounds. These combined sifters and mixers are well adapted for the manufacture of Seidlitz mixture, tooth-powder, compound liquorice powder, etc., without the annoyance of dirt and dust.

FIG. 88.



Harris' sifting machine.

Powdered drugs are frequently offered at prices lower than those asked for a good quality of the crude drug; yet it is well known that

Fig. 89.

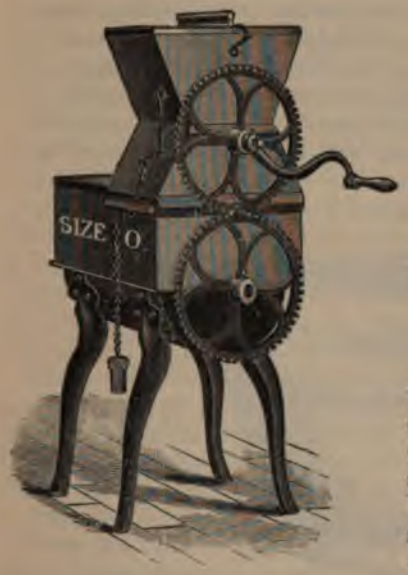


Fig. 90.

Jones' mixer and sifter.

the cost is enhanced by loss in drying, expense of powdering (from 3 to 10 cents per pound), and other incidentals. There can be but one explanation for this anomaly: either an inferior quality of drug has been ground, or admixtures have been made to increase the yield of the powder. As detection of the fraud is not within the reach of all, powdered drugs should be purchased only from dealers whose sense of truth and honor is paramount to their cupidity. Owing to the largely increased surface exposed to light and air in the case of powdered drugs, they are, as a rule, more liable to deterioration than crude drugs, and should therefore be more carefully protected, particularly against moisture.

Among other methods for the mechanical subdivision of drugs may be mentioned *trituration*, which consists in reduction of a substance to very fine powder by continued attrition of the particles between the hard surface of a pestle and the sides and bottom of a mortar. Trituration is usually applied to saline and similar chemical substances, and the mortars best adapted to the process are those made of Wedgewood ware, of the shape shown in Fig. 91. A rotary motion of the pestle accompanied by pressure is productive of the best results in trituration, the circles described being gradually enlarged from the centre outward and back again to the centre. A thin layer of the material should be kept between the pestle and the sides of the mortar. When the powder begins to cake and fall toward the centre of the mortar, a spatula should be run around the sides so as to loosen up and mix the different portions. The term trituration is also sometimes employed to designate the thorough mixture of vegetable or other

powders by rubbing them well together in a mortar; in such cases little if any pressure is employed, and thorough blending of the mixture is facilitated by frequently scraping the powder down from both pestle and mortar with a spatula.

The reduction of substances to fine powder by triturating them in the presence of a liquid having no solvent effect upon them, is termed *levigation*. The process is usually conducted in broad, shallow mortars. Formerly, when a stone slab and muller were employed, this method was also known as porphyrization, from porphyry, a very hard stone, the material of which the slab was made. Water, alcohol,

FIG. 91.

Wedgewood mortar and pestle.

or oil may be used as suitable media for levigation, the process consisting of the formation of a soft paste of the substance to be powdered and the liquid, this paste being then triturated or ground until perfectly smooth. Red mercuric oxide may thus be reduced to an impalpable powder by trituration with alcohol, and white paints, such as zinc oxide and lead carbonate, are ground smooth with oil in special paint mills.

Elutriation is a process intended for obtaining certain inorganic substances in a finely pulverulent condition, by diffusing them in water after they have been ground or crushed; the coarser particles then rapidly subside, owing to their higher specific gravity, while the water holding the fine powder in suspension is decanted and allowed to settle in another vessel, the decantation being repeated a second time if necessary. To facilitate drying of the elutriated powder, the magma or soft mass is drained as completely as possible, and then formed into small conical nodules, which are conveniently dried on warm porous tiles. The well-known soft prepared chalk, French bismuth subnitrate, and numerous lake colors, are obtained as fine powders by elutriation.

Other methods for the mechanical subdivision of drugs are *precipitation*, *reduction* and *granulation*.

By *precipitation* is understood the sudden destruction of the soluble form of a substance which is held in solution; this may be effected by the addition of another substance to the solution, or by some external agency. The substance thus thrown out of solution is termed the *precipitate*, and the substance or force causing the separation, the *precipitant*. Precipitation is employed in pharmacy as a method of pulverization and purification, and as a convenient means for obtaining many insoluble substances.

The first of these comes under the head of what may be termed simple or physical precipitation, usually brought about by the addition to the solution of some substance in which the dissolved body is insoluble; as in the precipitation of ferrous sulphate or of tartar emetic from aqueous solution by means of alcohol. Other examples of physical precipitation are the separation of iodine or camphor from alcoholic solution by the addition of water, the precipitation of solution of acacia by alcohol, the precipitation of lime-water by boiling, and the preparation of the official resin of jalap.

The process of precipitation when intended as a means of purification, or of the preparation of insoluble compounds, almost invariably involves chemical action, as in the purification of metals by electrolysis, the manufacture of mercuric iodide, etc.; in the former case simple decomposition of a salt is effected, while in the latter case mutual decomposition between two salts is as a rule necessary.

Some insoluble compounds are precipitated by simple decomposition of a substance by means of water, as bismuth subnitrate, yellow mercuric subsulphate, etc.; in the former case an acid solution is freely diluted with water, in the latter case white mercuric sulphate is thrown into boiling water.

Mercuric oxide can be obtained in a much finer state of division by precipitation than by any other method, but it must be brought about by chemical action. If a solution of mercuric chloride be poured into a solution of sodium or potassium hydroxide two new compounds, yellow mercuric oxide and sodium chloride, are formed, the latter remaining in solution, while the former separates as an impalpable powder, being insoluble in all neutral liquids. Lead iodide, magnesium carbonate, ammoniated mercury, and precipitated chalk are familiar examples of compounds prepared by chemical precipitation.

The character of the precipitate depends largely upon the conditions under which its formation is effected; thus, concentrated solutions are apt to yield dense precipitates, particularly if heat be employed, whereas cold dilute solutions, as a rule, produce light bulky precipitates. In the preparation of new chemical compounds by precipitation it is important that the proportion in which the precipitant is to be employed should be determined by calculation, as a deficiency or an excess may result in loss from imperfect precipitation or re-solution of the precipitate. Mutual decomposition between two salts always takes place in definite molecular propor-

tions, and the necessary quantities may be readily ascertained by writing out an equation showing the decomposition; thus the formation of yellow mercuric oxide is demonstrated by the equation $HgCl_2 + 2NaOH = HgO + 2NaCl + H_2O$, which shows that 1 molecule or 270.54 parts of mercuric chloride requires 2 molecules or 79.92 parts of sodium hydroxide for complete precipitation. In this case an excess of sodium hydroxide is not hurtful, but a deficiency would result in the production of mercuric oxychloride of brownish color instead of a pure yellow oxide. The equation $HgCl_2 + 2KI = HgI_2 + 2KCl$ shows that in the formation of red mercuric iodide 2 molecules or 331.12 parts of potassium iodide are necessary for the complete precipitation of 1 molecule or 270.54 parts of mercuric chloride; these proportions must be strictly observed, otherwise a loss will result, as red mercuric iodide is soluble in both potassium iodide and mercuric chloride solutions. When precipitation by mutual decomposition between two salts is proposed, the salts are mixed in the form of separate solutions, and perfect blending is accomplished by stirring the mixture.

The most convenient style of vessel for precipitation is a glass or stoneware jar considerably broader at the base than at the top, and provided with a lip; this greatly facilitates the subsidence of the precipitate, and the subsequent removal of the clear liquid remaining above the precipitate, known as *supernatant* liquid.

The purification of precipitates is effected by a process of washing, which consists either in mixing them repeatedly with fresh portions of water in a suitable jar, and decanting the supernatant liquid after it has become perfectly clear, or in continued affusions of water on the precipitate contained in a cloth strainer or paper filter; each portion of water should be well mixed with the precipitate and the washing continued until the complete removal of the soluble by-product has been ascertained by appropriate tests. When a precipitate tenaciously retains liquid, forming a thin paste, the mixture is termed a *magma*, and forcible expression must frequently be resorted to in order to remove the liquid, as in the case of washing ferric hydroxide, freshly precipitated calcium phosphate, etc.

The official reduced iron is an instance of a metal obtained in a finely divided state by *reduction;* ferric oxide being heated to redness in an atmosphere of hydrogen, in suitable tubes, and allowed to cool without contact of air. This method of producing metallic iron in fine powder yields better results than any other known.

Granulation is a process by which certain substances soluble in water are obtained in the form of coarse powder by simple evaporation of their solution, with constant stirring, until all moisture is dissipated. It is employed either for deliquescent and difficultly crystallizable substances, as potassium citrate and carbonate, or in cases where the solution, if allowed to evaporate very slowly, would yield larger crystalline masses, as ammonium chloride, lead acetate etc. Granulated powders, as the name indicates, never represent a

fine state of division, but offer a very convenient form for dispensing purposes. Zinc and tin may be readily granulated in the metallic state by heating them to a temperature a little below their melting-point, when they become very brittle, and can then be rubbed into coarse powder in a mortar.

Some substances obstinately resist pulverization by any of the methods mentioned, and require a different treatment; for instance, camphor cannot be reduced to a fine powder without being first brought to a state of partial or perfect solution by means of alcohol; a smooth paste being first formed of camphor and alcohol in a mortar, which is then triturated until perfectly dry and in the form of an impalpable powder—excessive pressure should be avoided during the trituration. Powdered camphor thus prepared is apt to return gradually to a crystalline condition, no matter how carefully it is preserved, but this can be prevented by precipitating the camphor in the presence of some powder with which it will become intimately mixed. Such a process was first published in Parrish's *Treatise on Pharmacy*, and is as follows: Four ounces of camphor dissolved in 8 fluidounces of alcohol are poured slowly, with constant stirring, into a smooth mixture of 15 grains of calcined magnesia and 2 pints of water; the precipitated camphor, enveloping the magnesia, soon rises to the surface, and is recovered by pouring the whole mixture on a paper filter, where it is allowed to drain. To facilitate drying of the mass, it is cut with a spatula into small particles, and is finally preserved in bottles. Although retaining a very small amount of moisture, this precipitated camphor keeps excellently, and may be used for all purposes requiring camphor, except cases of solution. Iodoform and boric acid can also be quickly reduced to an impalpable powder by trituration with alcohol, whereby partial solution is effected, and a dry powder is obtained upon evaporation of the alcohol. Friable substances, which are not held together by strong cohesive force, but the particles of which are apt to cake when submitted to pressure, may be powdered by simple friction over a perforated surface; no better method is known for obtaining magnesium carbonate in an impalpable condition than by rubbing the cakes over the surface of an inverted bolting-cloth sieve.

CHAPTER VII.

SOLUTION.

When a solid body is brought into contact with a fluid in such an intimate manner that it loses its original form and assumes that of the fluid, producing a clear and uniform liquid, the process is termed solution, as is also the newly-formed homogeneous liquid; but solution is by no means restricted to the liquefaction of solids by fluids, as gaseous and liquid substances can also be brought to the condition of perfect molecular blending characteristic of solution. The fluid used to produce solution is called a solvent or menstruum. The hypotheses at present engaging the minds of scientists regarding the electro-chemical decomposition of bodies in a state of solution need not be considered here; by some the process of solution is looked upon as one of great force and activity, and this view may in the course of time clear up many hitherto unexplained phenomena.

Two kinds of solution are recognized, namely, *simple* and *complex* solution; in the former the solvent produces no change in the sensible characteristics of the dissolved body, simply altering its physical condition, while in the latter, where solution takes place as the result of chemical action, the properties of both the solvent and the dissolved body become modified by the loss of old or the acquisition of new properties. In the case of a simple solution, the taste, odor, color, and chemical properties of the dissolved body remain intact and are imparted to the solution; as, for instance, solutions of sugar, table-salt, or potassium permanganate in water. In simple solutions the dissolved body can be recovered in its original condition by evaporation of the solvent. Complex solutions should not be confounded with compound solutions; the latter term indicates a mixture of solutions, which may all be simple in character, while complex solutions are understood to be the result of chemical action and are accompanied by one or more of the following phenomena: heat, effervescence, change of color, odor, and taste; as, for example, the solution of a Seidlitz powder or the solution of red mercuric oxide in nitric acid. The products obtained by evaporation of a complex solution will be found to have new properties, not possessed originally by the solvent or the dissolved body.

The greater the extent of surface exposed by the solid body to the liquefying action of the solvent, the more rapidly will solution be effected; hence mechanical division facilitates solution, because the latter process is in direct opposition to cohesion. A simple solution of solid substances may be considered as a fluid produced by the

intimate union of the solvent and the dissolved body in a state of minute division, the union and division being so complete that the forces of cohesion and gravity are suspended, otherwise a mixture only is produced, and the solid substance will again separate. The agitation of a mixture of a solid substance and solvent also causes more rapid solution, by constantly bringing fresh portions of the fluid into contact with the solid; if equal weights of acacia or sugar, in lumps or in fine powder, be placed in separate vessels with a sufficient quantity of water, the one being actively stirred while the other is allowed to remain at rest, solution will be completed in the former vessel long before it occurs in the latter; this is due to the fact that in the second vessel a dense solution will form immediately around the solid particles, and thus prevent the remainder of the fluid from exerting its solvent action.

The term "solubility," when no solvent is mentioned, always refers to the behavior of the substance toward water at the ordinary temperature, about 15.6° C. (60° F.); thus the statements that sugar is soluble and bismuth subnitrate is insoluble refer solely to the liquefying effect which water will have upon the two substances. Different degrees of solubility are expressed by such terms as *sparingly soluble*, *soluble*, and *very soluble*; these varying degrees of solubility do not determine the rapidity of solution, for some substances are known to dissolve slowly but to a greater extent than others which enter into solution more rapidly but in less proportion. Substances differ greatly in their solubility in water; as extremes may be mentioned zinc chloride, soluble in one-third of its weight of water, and barium sulphate, which requires about eight hundred thousand times its weight of water for solution. Substances but slightly soluble in water may be very soluble in other liquids; as camphor, which requires about 1000 parts of water for solution but is readily soluble in one-third of its weight of chloroform.

Heat, as a rule, favors the solution of solids and diminishes the solubility of gases, but there are no substances totally insoluble in the cold which become soluble by the aid of increased temperature. The effect of the application of heat is the establishment of currents in the liquid which will facilitate solution just as agitation of the vessel favors the same result; and moreover, since heat intensifies molecular motion in both the menstruum and the solid, not only will an increased quantity of the latter assume the fluid state, but solution will also be effected in less time, on account of the energetic intramolecular activity. There are some exceptions to the general rule that heat increases the solubility of substances; for instance, common salt is about as soluble at ordinary temperatures as at the boiling-point of water; sodium sulphate or Glauber's salt increases in solubility rapidly from 15° C. (59° F.) to 34° C. (93.2° F.), at which point water takes up four times its weight of the salt, but beyond this temperature its solubility again decreases until 100° C. (212° F.) is reached, when water takes up about 2.13 times its weight of the salt;

calcium citrate and sulphate as well as slaked lime are far less soluble in hot water than in cold, and will be readily deposited if their solutions be boiled.

The Pharmacopœia, in the case of nearly every soluble substance, indicates the degree of solubility by stating the number of parts by weight of the solvent necessary to dissolve one part of the substance; this proportion is usually given for both normal and boiling temperatures. The pharmacist must be familiar with the methods for determining the solubility of substances, so as to be able to apply the official tests intelligently. At ordinary temperature, 15° C. (59° F.), a simple but accurate plan is to place some of the substance in fine powder in a wide test-tube, or small flask, provided with a stopper, and add as much of the solvent as may be necessary, leaving, however, a small portion of the substance undissolved—shake the flask freely, or stir the contents of the tube briskly with a glass rod, warm the mixture slightly in a water-bath and allow it to cool down to 15° C. (59° F.), by placing the tube or flask in water having that temperature. In order to avoid a supersaturated solution, the mixture should next be set aside for twenty-four hours at normal temperature, and occasionally stirred with a glass rod, the sides of the tube or flask being also rubbed with the rod. The solution thus obtained is passed through a small dry filter into a tared glass or porcelain dish, and weighed; after evaporation to dryness, the residue is carefully weighed, when the difference between the weight of the solution and that of the dry residue represents the weight of solvent, and from this the ratio of solubility is easily calculated. Example: Suppose the clear filtrate weighs 10.5 Gm. (or 162 grains) and the dry residue therefrom 1.125 Gm. (or 17.36 grains), then the weight of the solvent must be 9.375 Gm. (or 144.64 grains), and the substance under examination is soluble in 8.33+ parts of the liquid used, for $9.375 \div 1.125$ or $144.64 \div 17.36 = 8.33+$.

The determination of the solubility of a substance at temperatures above the normal becomes more difficult on account of the loss incurred during the filtration of hot liquids by ordinary methods. Dr. Charles Rice has devised a very useful and simple apparatus, called by him a lysimeter (from the Greek λύσις, solution), which enables the operator to obtain a clear filtrate without any loss whatever, even at the boiling temperature of liquids. Fig. 92 shows the construction of the lysimeter, which consists of a glass tube, *a*, 15 centimeters (6 inches) in length and 1 centimeter ($\frac{3}{8}$ inch) in external diameter, provided at one end with a well-ground stopper, *c*, while the other end is cup-shaped, there being a contracted neck between the cup and the main tube. Into this cup is made to fit a carefully ground glass bell, *e*, having a small perforation in its bottom, as shown in *f*; there is also a stopper, *b*, which is carefully ground to fit into the cup, and which is inserted after the glass bell, *e*, has been removed.

When using the apparatus it is necessary to provide sufficient liquid to allow at least one-half of the tube, *a*, to be immersed; beaker glasses, or preferably wide test-tubes, may be used for effecting the solution. Suppose it is desired to ascertain the solubility of a substance in boiling alcohol. The following is the plan of procedure: Insert the stopper, *c*, into the tube, *a*, and into the cup-shaped end insert the glass bell, *e*, containing a pledget of purified cotton, and secured in place by a thin platinum wire passing around the contracted neck and over the mouth of the bell. Sufficient alcohol having been put into a wide test-tube or a beaker, the same is heated in a water-bath and the finely-powdered substance added until, after boiling has continued for some time, a portion of the substance remains undissolved. The lysimeter, prepared as above directed, is now inserted into the liquid, and when the tube has assumed the temperature of the boiling liquid the stopper, *c*, is removed, which allows the solution to filter through the pledget of cotton and rise in the tube as far as the quantity of fluid will permit. If the filtered solution be allowed to flow back through the cotton once or twice, greater uniformity of the liquid will be insured. The stopper, *c*, is now reinserted, the apparatus withdrawn from the liquid and turned upside down to allow the bell, *e*, to be removed and the stopper, *b*, to be inserted in its place. The stoppered tube is carefully cleaned externally by washing with alcohol, and laid aside until cold. The tare of the stoppered tube having previously been ascertained, the increase in weight must represent the weight of the solution contained therein. After transferring the solution to a tared capsule or beaker, the tube is carefully rinsed with alcohol, and the washings added to the contents of the capsule or beaker; the solution is slowly evaporated on a water-bath, and afterward heated to dryness in a drying oven, when the weight of the residue will indicate the weight of the dissolved substance, and subtracting this from the weight of the solution gives the weight of alcohol. From these data the ratio of solubility is calculated in the manner already explained in the example given for determining the solubility at normal temperature.

FIG. 92.

Dr. Rice's lysimeter.

Rapid simple solution of solid bodies is always accompanied by a

fall in temperature, while a solution of gases causes a rise in temperature; these phenomena are in accordance with the laws governing the state of aggregation of bodies. Solids, for the assumption of the fluid state, require a certain amount of heat, which is withdrawn from the surrounding liquid and becomes latent, while gases when condensing to liquids give out an amount of heat corresponding to that required for the gaseous state. Four ounces of ammonium nitrate or potassium iodide rapidly shaken in a bottle with two ounces of pure water will produce sufficient cold to condense the moisture of the air on the outside of the bottle and freeze it into thin sheets of ice.

SATURATED SOLUTIONS, in a pharmaceutical sense, are such as cannot take up any more of the dissolved body at ordinary temperature, in other words, the solvent has become charged with as much soluble matter as it is capable of retaining in intimate union at the ordinary temperature. The statements of ratio of solubility in the Pharmacopœia and elsewhere always refer to the formation of saturated solutions at the temperature named; thus the official statement that cane sugar is soluble at 15° C. (59° F.) in ½ part of water and 175 parts of alcohol, in ⅓ part of boiling water and 28 parts of boiling alcohol, means that, with the proportions of water, and alcohol named, sugar forms saturated solutions at the temperatures indicated. Supersaturated solutions are those in which the solvent, by artificial means, has been made to take up more of the soluble matter than it is capable of retaining under ordinary circumstances; they are very unstable and present a peculiar condition of solubility. If three parts of sodium sulphate be dissolved in one part of water at 30° C. (86° F.), the solution carefully filtered into a perfectly clean dry bottle free from dust, and allowed to cool down gradually, it will remain clear as long as it is not disturbed, although supersaturated, since water at 15° C. (59° F.) can dissolve only about one-third of its weight of the salt; but, if the bottle containing the supersaturated solution be shaken, or a little broken glass be introduced, the whole contents will suddenly congeal to a crystalline mass. Saturated solutions of salts are frequently capable of dissolving other salts, and thus may be used for purposes of purification; if potassium nitrate be treated with a saturated aqueous solution of the same salt no more potassium nitrate can be taken up, but impurities present will enter into solution and are thus removed.

The effect which the presence of one substance may have upon the solubility of another is interesting as well as of practical value in pharmacy; frequently the increased solubility thus produced is due to a chemical reaction between the two substances. Thus corrosive sublimate is far more soluble in water in the presence of alkali chlorides, and red mercuric iodide is readily dissolved in a solution of potassium iodide; in both cases union takes place between the mercuric and alkali salts. The increased solubility of potassium chlorate in the presence of sodium bicarbonate is well known; mutual decomposition, no doubt, results—the newly formed salts,

sodium chlorate and potassium bicarbonate, requiring only 1.1 part and 3.2 parts of water at 15° C. (59° F.) respectively for solution, as against 16.7 and 11.3 parts for the original salts. Ordinarily iodine requires about 5000 parts of water for solution, but if mixed with twice its weight of potassium iodide, will readily dissolve in 20 times its weight of water. In this case no chemical union takes place, as the iodine has every appearance of being dissolved but not combined; it retains its characteristic color and odor, and if the solution be heated in a test tube, the iodine can be completely volatilized, a portion resubliming in the cooler part of the tube in its original condition.

Since rapid simple solution causes a decided fall in temperature, advantage is taken of the fact that some substances hasten the liquefaction of others in the production of so-called freezing-mixtures; thus, 5 parts each of ammonium chloride and potassium nitrate dissolved in 19 parts of water will cause a drop in temperature of 20° C. (36° F.); a mixture of 2 parts of snow and 3 parts of crystallized calcium chloride will cause the temperature to fall from 0° C. (32° F.) to —45.5° C. (—50° F.) and freeze mercury; the usual mixture for ice-cream freezers consists of salt with twice its weight of snow or crushed ice, which produces a temperature equal to about —20° C. (—4° F.), the cream in the cylinder freezing by reason of the great abstraction of heat necessary for the rapid liquefaction of the ice and snow surrounding it—not, as some persons imagine, because intense cold is imparted to it from the outside.

Anhydrous salts, that is, salts completely deprived of water, will frequently cause a rise in temperature when brought into solution; the heat thus generated must be looked upon as due to chemical action caused by the water in restoring the anhydrous salt to the crystallized state. If crystallized sodium carbonate be shaken with twice its weight of water a marked fall in temperature will be noticed, whereas anhydrous sodium carbonate shaken with twice its weight of water causes a rise in temperature, thus proving the correctness of the preceding supposition. When liquids are dissolved in other liquids, no change of temperature will occur in the mixture unless contraction of volume takes place, as in the case of alcohol and water or sulphuric acid and water.

The simplest way of effecting solution of solids is to bring them in the form of powder into contact with the solvent in such a way that frequent agitation of the mixture is possible; for saline and similar substances a porcelain or Wedgewood mortar, which admits of active trituration, is best adapted. Considerable saving of time may be effected in the solution of larger quantities of solids, if the powdered substance be repeatedly triturated with fresh portions of the solvent, each portion of solution being poured off when saturated. Small quantities of readily soluble substances, such as potassium iodide and bromide, silver nitrate, zinc sulphate and the like, may be placed directly in a bottle with the solvent, and the mixture agitated

until perfect solution results. Some substances, of hygroscopic or deliquescent character, are preferably not reduced to powder before adding the solvent, in order to avoid agglutination; such are the official scale salts of iron, which will dissolve more speedily if shaken with water in scale form than in fine powder. Whenever heat must be employed for small operations of solution, a glass flask will be found more desirable than a dish, as evaporation of the solvent will be retarded, and consequently the heat become concentrated in the vessel. Solutions of solids are known to be denser than the solvents used in preparing them, and advantage is frequently taken of this fact to facilitate the solution of large quantities of solid substances, or of such as are liable to form viscid solutions, or where stirring or agitation is impracticable, by what is commonly known as *circulatory displacement*, which consists in suspending the soluble matter just below the surface of the solvent, either on a porous diaphragm, in a bag of loosely textured cloth, or in a perforated vessel, which should be moved about from time to time. By this arrangement, that portion of the solvent least charged with soluble matter is always in contact with the solid, and as the solution becomes saturated it sinks to the bottom, displacing the portion less charged with the solid, which rises to the surface, and thus a continual circulation or system of currents, favorable to rapid solution, is kept up in the fluid.

Percentage Solutions. This term is applied to solutions of definite strength, containing a specified amount of soluble matter in one hundred parts of the solution: for solids and gases percentage solutions should always be prepared by weight, while for liquid substances either weight or volume may be employed. The quantity of soluble substance and solvent necessary to make a specified quantity of any particular percentage solution may be readily ascertained by the following rule: *Multiply the quantity of solution desired, in grammes or grains, by the number expressing the percentage, divide the product by* 100, *and the quotient will indicate the quantity of soluble substance necessary; subtract this from the total quantity of solution desired, and the remainder will indicate the necessary quantity of solvent.*

Examples: Wanted 500 Gm. of 10 per cent. carbolized oil: $500 \times 10 = 5000$ and $5000 \div 100 = 50$; $500 - 50 = 450$. Answer: Dissolve 50 Gm. of crystallized carbolic acid in 450 Gm. of olive oil.

Wanted 750 grains of 4 per cent. cocaine hydrochloride solution; $750 \times 4 = 3000$ and $3000 \div 100 = 30$; $750 - 30 = 720$. Answer: Dissolve 30 grains of cocaine hydrochloride in 720 grains of distilled water.

Wanted 640 Gm. of 2 per cent. mercuric chloride solution: $640 \times 2 = 1280$ and $1280 \div 100 = 12.8$; $640 - 12.8 = 627.2$. Answer: 12.8 Gm. of mercuric chloride must be dissolved in 627.2 Gm. of distilled water.

Wanted 480 grains of 20 per cent. quinine oleate: $480 \times 20 = 9600$ and $9600 \div 100 = 96$; $480 - 96 = 384$. Answer: Dissolve 96 grains of quinine alkaloid in 384 grains of oleic acid.

Sometimes a percentage solution of two or three substances is wanted; in such a case the absolute quantity of each active ingredient is first ascertained by the rule given above; the sum of their weights is then subtracted from the total quantity of solution desired to find the necessary weight of the solvent; for instance: Wanted 240 grains of 8 per cent. cocaine hydrochloride solution, containing also 2 per cent. of boric acid: $240 \times 8 = 1920$ and $1920 \div 100 = 19.2$; $240 \times 2 = 480$ and $480 \div 100 = 4.8$; $19.2 + 4.8 = 24$; $240 - 24 = 216$. Answer: Dissolve 19.2 grains of cocaine hydrochloride and 4.8 grains of boric acid in 216 grains of distilled water.

When a definite volume of a weight percentage solution is wanted, the quantity nearest in volume to that required must be made; although this sometimes involves a slight loss, there is no other method known if accuracy is to be preserved. Thus, if 2 fluidrachms of a 4 per cent. solution of any soluble chemical are wanted, 5 grains of the substance must be dissolved in 120 grains of water; the 125 grains of solution will measure slightly more than 2 fluidrachms, but the excess, which is slight, can be rejected. If 8 fluidounces of a 10 per cent. solution are wanted, 4100 grains of solution must be made by using 410 grains of the medicinal agent and 3690 grains of water; 8 fluidounces of water weigh 3646 grains, hence the excess of solution will not be large. If a quart of 1 per cent. mercuric chloride solution is desired, 15,000 grains of solution must be made, as the weight of a quart of water is 14,583 grains, which is only 267 grains less than the quantity of water necessary; 150 grains of mercuric chloride dissolved in 14,850 grains of water yield only a little over ½ fluidounce more of the solution than is wanted. If 500 Cc. of a 5 per cent. solution are desired, 530 Gm. of the solution must be made, the excess of solution being 4.5 Cc., for 5 per cent. of 530 is 26.5, and as each Cc. of water equals 1 Gm., $530 - 26.5 = 504.5$. When solvents other than water are used, having a higher or lower specific gravity, due allowance must be made for this fact, as also when strong solutions of substances likely to increase the volume are to be prepared.

The liquids used as solvents or menstrua in pharmacy, are water, alcohol, ether, vinegar, glycerin, and occasionally fixed and essential oils; each of these fluids has a specific action, and their use gives rise to different classes of solution designated as infusions, tinctures, wines, etc. *Water* is more extensively employed than any other solvent; nearly all the salts of the alkalies, earths, and metals are dissolved by it, together with a large number of vegetable acids and the salts of the alkaloids. *Alcohol* is an excellent solvent for vegetable substances, such as resins, volatile oils, glucosides, and alkaloids; it also possesses valuable negative properties, since it does not dissolve gum, starch, and albumen, which impair the stability of aqueous solutions. The combined solvent powers of alcohol and water are utilized in the form of diluted alcohol and wine as a men-

struum for numerous liquid vegetable preparations. The use of *Ether* is confined to solutions of fixed oils and fats, volatile oils and resins, and a few alkaloids and neutral principles. *Glycerin* is chiefly employed to insure the permanency of vegetable solutions when the use of alcohol is contra-indicated; it is also an excellent solvent for the tannins, pepsin, and some mineral salts and vegetable acids, and forms the basis of a valuable class of solutions known as *glycerites*.

Complete solution is generally aimed at in pharmacy in the case of inorganic solids, but is frequently impossible with substances of vegetable origin.

The process of treating a mixture of soluble and insoluble mineral substances with solvents which only partially dissolve them is termed *lixiviation* or *leeching*, and is extensively practised in the arts; as an example may be cited the leeching of ashes of wood and marine plants for the purpose of dissolving out the alkali carbonates, iodides, etc. The various methods of partial solution applied to mixtures of soluble and insoluble vegetable matter are usually comprised under the general term "extraction," but have received specific names, such as infusion, decoction, maceration, digestion, and percolation.

The process of *Infusion* is understood to represent the solvent action of boiling water, on vegetable drugs, during the time occupied in cooling; it may be varied, as to a longer or shorter period of time, according to the degree of extractibility of the principles to be dissolved, and should always be conducted in closed vessels. The substance to be infused should be in a coarse state of division and preferably suspended in the liquid. *Decoction* represents the solvent action of fluids at their boiling temperature, and is confined to drugs not yielding their active virtues at a lower temperature and where no loss of volatile principles need be feared. *Maceration* consists in subjecting a mixture of soluble and insoluble matter in a divided state to the solvent action of fluids at the common temperature for such length of time as may be necessary to insure complete solution of the principles sought; the process must be conducted in well-closed vessels, and the contents must be well shaken at least once in twenty-four hours. Frequent agitation is essential if complete extraction of soluble matter is to be insured by maceration, as otherwise a dense layer of a concentrated solution will soon envelop the material and prevent the solvent action of the menstruum from being effective; hence only a small proportion of the soluble constituents will be taken up, as may be readily observed in the slight color and odor of the supernatant liquid, if a mixture of asafetida and alcohol, or of opium and water, be set aside for a week *without agitation*. *Digestion* differs from maceration only in the higher degree of temperature employed, it being constant during the process, the use of which is confined to substances of very close texture.

CHAPTER VIII.

PERCOLATION.

PERCOLATION, or, as it is sometimes called, displacement, is beyond doubt the most important method of solution or extraction in the hands of the pharmacist. The term percolation (from the Latin words *per* and *colo*, meaning to strain or trickle through) may be defined as a process whereby the soluble constituents of vegetable drugs are extracted by allowing the menstruum to permeate a column of the powdered material, the saturated solution, as fast as formed, being removed, thus continually presenting fresh solvent to the drug. The apparatus in which the process is carried on is known as the *percolator*, the solution obtained as the *percolate*, and the residue of insoluble matter as the *marc*.

Although the idea of solution by percolation did not originate in this country, its present improved and general application is due entirely to American enterprise and ingenuity. The first attempt to extract soluble matter from powdered drugs by allowing a menstruum to exert its solvent action during its passage through a column of the material was made by Count Real in the early part of the present century, the principle involved being about the same as that utilized by the French in the preparation of their world-renowned coffee. In 1833, M. Boullay, an enterprising French pharmacist, considerably modified the plan of Count Real, and in a series of carefully conducted experiments demonstrated the adaptability of the process of percolation to the extraction of vegetable drugs. So convincing were the results of his investigations that Prof. Procter and A. Duhamel, prominent American pharmacists, became deeply interested in the work, and in 1839 strongly advocated its adoption as a method of extraction superior to others known at that time. Although the process of percolation was recognized in the United States Pharmacopœias of 1840 and 1850, it did not meet with the general favor since accorded it until Prof. Israel Grahame, of the Maryland College of Pharmacy, in 1858, suggested some valuable improvements, which led to better results than had yet been obtained. To Prof. Grahame belongs the credit of first advocating the use of powders of uniform degree of fineness as well as the proper moistening of the powdered drug with a sufficient quantity of the menstruum before packing it in the percolator, both of which suggestions are now considered indispensable to successful percolation; at the same time, the use and advantage of a common funnel for the percolation of many drugs was pointed out. The advantage of properly moistening the powdered drug before packing

will be readily understood when it is considered that the material to be operated upon is not a mere mechanical mixture of soluble and insoluble matter, but that the soluble principles to be extracted are intimately held or enclosed by the insoluble cellular tissue, and that penetration of the tissue by the menstruum is necessary to effect solution; the saturation of the powder with the liquid prepares the constituents for ready solution and establishes an affinity between the cellular contents and the fresh menstruum, enabling the latter to permeate the cells by osmotic action. If the menstruum is brought in contact with dry powder, absorption of the former either takes place very slowly or is entirely interfered with, just as dry, hard sponge resists the entrance of water for a long time; the original moist condition of the drug before it was powdered must therefore be re-established before the menstruum can exercise its power of extraction.

The principle underlying the process of percolation may be stated as follows: A solvent or menstruum, poured on the top of a mass of powder consisting in part of soluble matter, supported on a porous diaphragm in a cylindrical or conical vessel, descends from layer to layer by reason of its own gravity and the pressure of the superincumbent liquid, penetrating the particles of powder by reason of surface action, and exercising its solvent power on each successive layer until its power of solution is exhausted, after which it continues its downward flow, as a saturated solution, into the receiving vessel below. This process continues until all soluble constituents have been removed from the powder, the descending menstruum becoming less and less charged with extractive matter. To insure such complete extraction it is absolutely necessary that the material operated upon shall be in a uniform powder and that the capillarity or porosity of the mass be not interfered with in any way, so that the descent of the menstruum may be slow, even, and regular from one horizontal layer to the next.

Different styles of percolators have been proposed at various times, and as drugs vary in their nature and require different treatment to yield different preparations, the pharmacist must be supplied with a variety of percolators, from the conical shape of the ordinary funnel to the nearly cylindrical. The choice of percolator depends largely upon the character of the percolate to be obtained, and also upon the nature of the drug; for instance, if a very strong solution is to be prepared with a minimum quantity of menstruum, a narrow cylindrical percolator is preferable, so that the solvent is made to pass through a long column of the drug and thus become thoroughly saturated; a cylindrical, or only slightly tapering, percolator is also indicated when the menstruum is strongly alcoholic, or when ether or some other volatile liquid is used for extraction. Figs. 93 and 94 represent two very useful percolators for the preparation of fluid extracts and tinctures. If, on the other hand, the quantity of drug to be extracted is small in proportion to the menstruum, as in the majority of official tinctures, a wider percolator, of the shape and

style shown in Fig. 95, may be used, in which the liquid will traverse the column of drug more rapidly and yet be able to exhaust it thoroughly, owing to the larger amount of menstruum at the disposal of the operator. When drugs such as gentian, senega, rhubarb, orange-peel, and others, which have a tendency to swell considerably, particularly with aqueous or feebly alcoholic menstrua, are to be percolated, a common funnel will often be found

FIG. 93.

Glass percolator described in the U. S. Pharm., 1890.

FIG. 94.

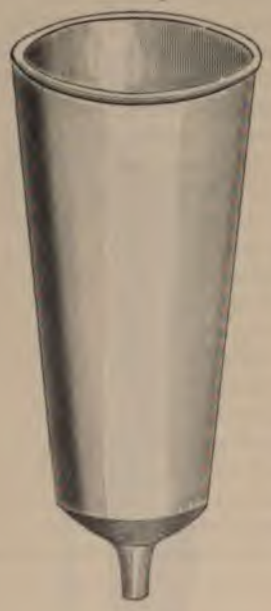
The Oldberg percolator.

advantageous on account of the ample allowance for lateral expansion of the moist drug. The size of the percolator selected should be in proportion to the quantity of drug to be extracted; when properly packed in the percolator the drug should not occupy more than two-thirds of its height.

The common tin percolator (Fig. 96) consists of a cylinder varying in size and tapering somewhat toward the funnel-shaped end, provided with two perforated diaphragms fitting loosely into the cylinder, the lower of which should be more finely perforated than

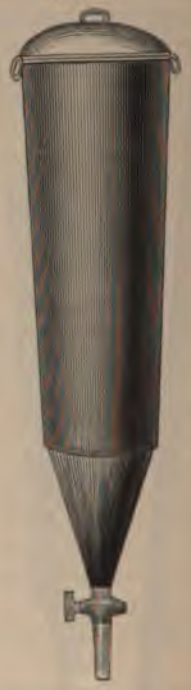
the upper. The stopcock in the neck of the funnel serves the double purpose of allowing maceration for any desired period and of enabling the operator to regulate the rate of flow of the percolate. Tin percolators cannot be used, however, for any drugs containing principles liable to be affected by metal, or to be exhausted with acid menstrua.

FIG. 95.



Ordinary glass percolator.

FIG. 96.



Covered tin percolator with stopcock for regulating the flow.

For percolation with very volatile liquids—ether, chloroform, and the like—a specially constructed percolator must be used (see Fig. 97), in which proper provision is made to prevent loss of menstruum and to establish communication between the vessel intended to receive the percolate and the space above the drug in the percolator, so that the air may pass upward when displaced by the percolate in the receiving jar; this latter provision is essential to successful percolation. As may be seen from the illustration, the percolator is fitted air-tight to the receiving vessel by being passed through a cork, and loss of menstruum at the top is prevented by a water-joint with which the cover of the percolator forms an air-tight connection. The air is carried up outside of the percolator, and made to enter at the top, to take the place of menstruum pass-

ing downward through the drug. Fresh menstruum may be supplied through the opening in the cover without disturbing the water-joint. Another plan to provide for the upward displacement of the air from the receiving jar is to pass a tube through the centre of the percolator and extending below the lower diaphragm, the drug being packed around the tube; such an arrangement is shown in the tin percolator, Fig. 98, which is likewise provided with a water-joint, and the exit tube of which should also pass air-tight through a cork in the neck of the receiving vessel. An arrangement of tubing on the outside, as seen in Fig. 97, may be attached to any percolator capable of being closed air-tight at the top with a cork.

Fig. 97.

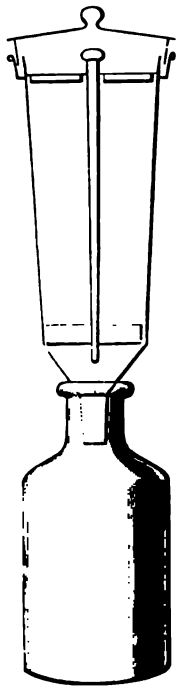
Glass percolator for use with volatile menstruum.

In 1874 the Dursse percolator was introduced (see Fig. 99). It combines the advantages of a broad cylindrical and a conical vessel, and is admirably adapted for quantities of drug ranging from 400 to 600 Gm. Unfortunately but one size is made of this pattern, which is 15 inches in length, 5 inches in diameter at the top and 1 inch at the beginning of the outlet tube. One of these percolators was in use almost weekly, during eighteen years, in the author's hands, and many a pound of nux vomica, cinchona, ergot, ginger, vanilla, gentian, rhubarb, valerian, etc., was successfully extracted therein during that time. Its chief merits lie in the perfect uniformity of its sides and its accurately fitting cover, by which the flow of the liquid can be regulated and all volatilization of menstruum be prevented. Being made of heavy glass it bears usage very well and is not easily broken.

Manufacturers who operate upon large quantities of drugs, varying from 25 to 500 pounds or more, employ percolators made of heavy tin or tinned copper. Such percolators are usually of the shape shown in Fig. 100, and supported in an adjustable frame, or are cut off flat at the point where the funnel-shaped end begins, and supported on a heavy wooden stand. In the latter shape, the drip-cock is situated on the side of the percolator, near the bottom. These large percolators are provided with two diaphragms or perforated disks, likewise made of heavy tin; the one is placed about eight or ten inches from the bottom, and is usually covered with a piece of muslin before the moistened

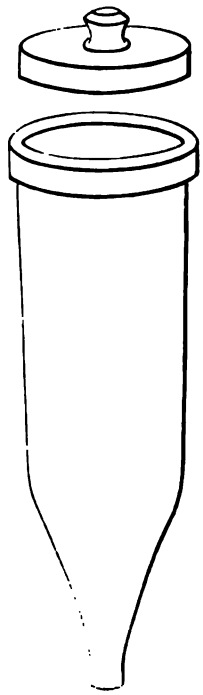
drug is introduced, while the other diaphragm is inserted over the mass of drug, which has been previously covered with a piece of felt or flannel, to insure uniform distribution of the menstruum. In order that the descent of the menstruum may be regular and uninterrupted during maceration of the drug, a tube attached to the inner side of the percolator, connects the space below the lower diaphragm with the space above the upper disk, and thus allows the

FIG. 98.



Tin percolator for volatile liquids.

FIG. 99.



The Durrse percolator.

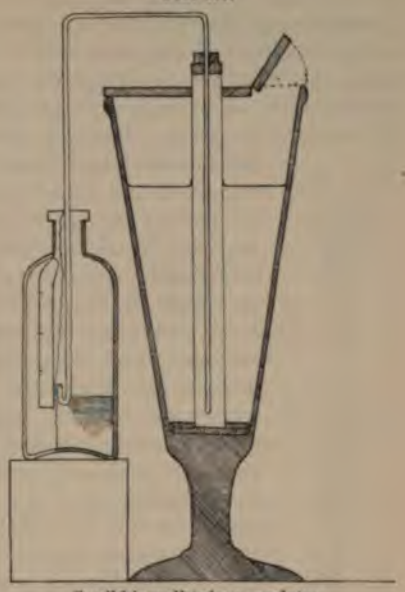
air from below to displace the menstruum above. A well-fitting cover, as shown in the illustration, prevents evaporation of alcohol and admits fresh menstruum when desired.

The well-known siphon or well-tube percolator, first suggested in 1872 by Dr. E. R. Squibb, is still in constant use in his laboratories; the principle involved, with slight modifications, has been adopted in the official directions for percolation in the United States Pharmacopæia for 1880 and 1890. The Squibb well-tube percolator, as shown in Figs. 101 and 102, is constructed upon the principle of an artesian well, the moistened drug representing the soil through which the menstruum passes very slowly, the solution or percolate, rising in the well-tube which passes through the centre of the mass, being finally drawn

FIG. 100.

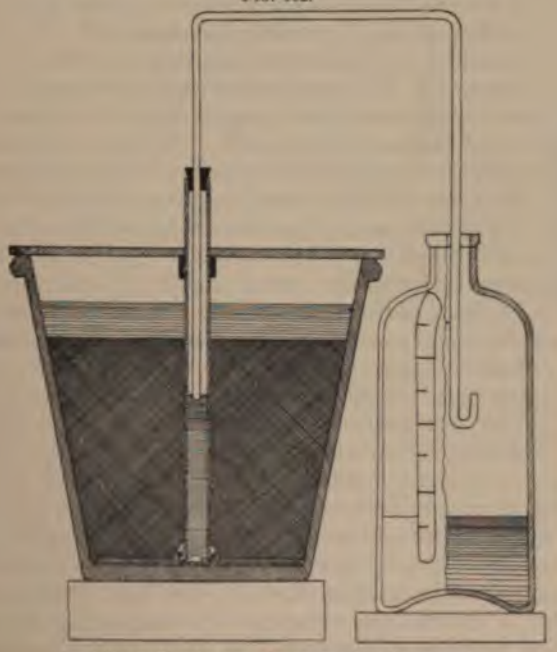
Copper percolator, tinned inside. (Capacity, 20 to 100 gallons.)

FIG. 101.



Squibb's well-tube percolator, made of glass.

FIG. 102.



Squibb's well-tube percolator, made of stoneware.

off by means of the glass siphon. The process is completely under the control of the operator as regards the rate of flow of the percolate and maceration of the mass to any desired extent. To prevent particles of drug from entering the well-tube, this is made to rest on several disks of flannel, through which the percolate must pass before it can enter the tube. The siphon acts automatically after it has once been started, and cannot exhaust itself, because, when the liquid in the percolator falls to the level of the turned-up end of the outer limb of the siphon, the flow ceases, leaving the siphon-tube full of liquid, the difference in the length of the two limbs of the siphon being only such that the inner limb reaches the bottom of the well-tube, and when measured on the outer limb, reaches to one-half of its turned-up end. The pressure on the surface of the moistened drug being duly counterbalanced by the atmospheric pressure on the column of percolate in the well-tube and siphon, all particles of the mass in the percolator will be subject to uniform pressure; thus the gravitation of the liquid is used to best advantage, just as in the case of the rubber tube recommended in the pharmacopœial directions for percolation. The body of the percolator is made of glass or stoneware, and the evaporation of menstruum is prevented by a tightly-fitting cover of sheet rubber about ¼ inch thick.

Fig. 103.

During the past ten or twelve years much has been written about "pressure percolators," the chief claim advanced for their use being the complete extraction of drugs with less menstruum than by ordinary methods, which applies to the preparation of concentrated solutions, such as fluid extracts. The idea of more complete solution by means of pressure originated with Count Real about 1815, and the apparatus devised by him (see Fig. 103) bears a close resemblance to some of the pressure percolators of the present day, devised by Rosenwasser, Berry, Suit, and Anderson. In the new apparatus the drug to be extracted is confined, by means of a suitable screw arrangement, between perforated disks, in any desired space, without the possibility of expansion on coming in contact with the bulk of the menstruum. The solvent is forced through the mass by pressure obtained from a column of liquid 10 or 12 feet in height, supplied by a reservoir.

Management of the Process of Percolation. The Pharmacopœia gives the following directions for conducting percolation, which are applicable to all official preparations in which this method of solution is indicated, as in each individual case the fineness of powder, the quantity of menstruum to be used for moistening the drug, and the degree of firmness with which it is to be packed, are specified:

"The percolator most suitable for the quantities contemplated by the Pharmacopœia, should be nearly cylindrical or slightly conical, with a funnel-shaped termination at the smaller end. The neck of this funnel end should be rather short, and should gradually and regularly become narrower toward the orifice, so that a perforated cork, bearing a short glass tube, may be tightly wedged into it from within until the end of the cork is flush with its outer edge. The glass tube, which must not protrude above the inner surface of the cork, should extend from 3 to 4 Cm. beyond the outer surface of the cork, and should be provided with a closely-fitting rubber tube, at least one-fourth longer than the percolator itself, and ending in another short glass tube, whereby the rubber tube may be so suspended that its orifice shall be above the surface of the menstruum in the percolator, a rubber band holding it in position.

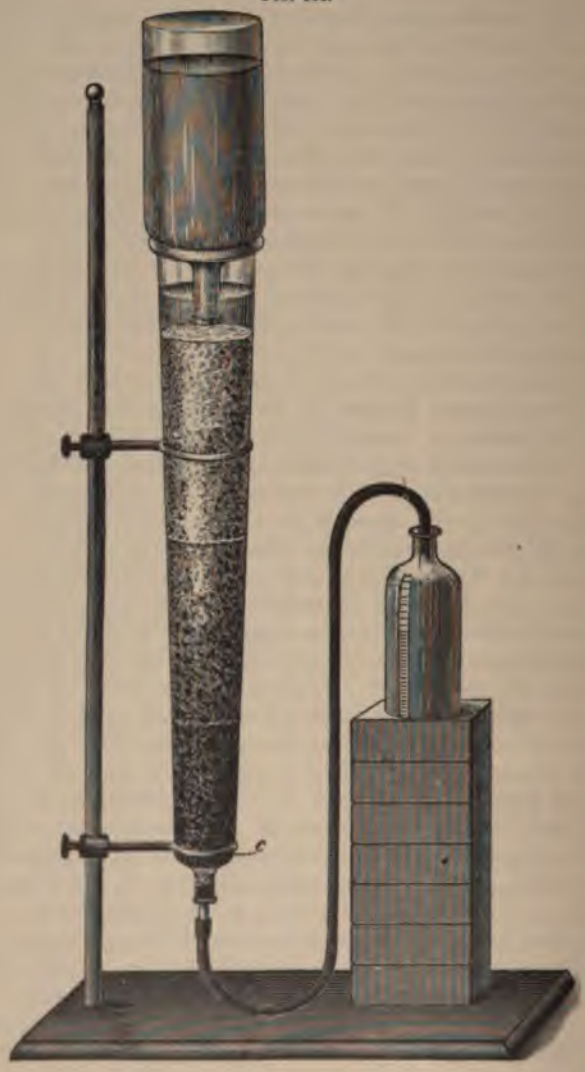
"The percolator is prepared for percolation by gently pressing a small tuft of cotton into the space of the neck above the cork, and a small layer of clean and dry sand is then poured upon the surface of the cotton to hold it in place.

"The powdered substance to be percolated (which must be uniformly of the fineness directed in the formula, and should be perfectly air-dry before it is weighed) is put into a basin, the specified quantity of menstruum is poured on, and it is thoroughly stirred with a spatula or other suitable instrument until it appears uniformly moistened. The moist powder is then passed through a coarse sieve—No. 40 powders, and those which are finer, requiring a No. 20 sieve, whilst No. 30 powders require a No. 15 sieve for this purpose. Powders of a less degree of fineness usually do not require this additional treatment after the moistening. The moist powder is now transferred to a sheet of thick paper and the whole quantity poured from it into the percolator. It is then shaken down lightly and allowed to remain in that condition for a period varying from fifteen minutes to several hours, unless otherwise directed; after which the powder is pressed by the aid of a plunger of suitable dimensions, more or less firmly in proportion to the character of the powdered substance and the alcoholic strength of the menstruum; strongly alcoholic menstrua, as a rule, permitting firmer packing of the powder than those weaker. The percolator is now placed in position for percolation, and the rubber tube having been fastened at a suitable height, the surface of the powder is covered by an accurately fitting disk of filtering paper or other suitable material, and a sufficient quantity of the menstruum poured on through a funnel reaching nearly to the surface of the paper. If these conditions are accurately observed the menstruum will penetrate the powder equally until it has passed into the rubber tube, and has reached in this a height corresponding to its level in the percolator, which is now closely covered to prevent evaporation. The apparatus is then allowed to stand at rest for the time specified in the formula.

"To begin percolation, the rubber tube is lowered and its glass

end introduced into the neck of the bottle previously marked for the quantity of liquid to be percolated, if the percolate is to be measured, or of a tared bottle if the percolate is to be weighed; and by raising

FIG. 104.



or lowering this recipient the rapidity of percolation may be increased or lessened as may be desirable—observing, however, that the rate of percolation, unless the quantity of material taken in operation is largely in excess of the pharmacopœial quantities, shall not exceed

the limit of ten to thirty drops in a minute. A layer of menstruum must constantly be maintained above the powder, so as to prevent the access of air to its interstices, until all has been added or the requisite quantity of percolate has been obtained. This is conveniently accomplished, if the space above the powder will admit of it, by inverting a bottle containing the entire quantity of menstruum over the percolator in such a manner that its mouth may dip beneath the surface of the liquid, the bottle being of such a shape that its shoulder will serve as a cover for the percolator. (For illustration of the official process, see Fig. 104.)

"When the process is successfully conducted, the first portion of the liquid or percolate passing through the percolator will be nearly saturated with the soluble constituents of the substance treated; and if the quantity of menstruum be sufficient for its exhaustion, the last portion of the percolate will be destitute of color, odor, and taste other than that possessed by the menstruum itself."

The degree of fineness of powder to which a drug is to be reduced depends partly upon the menstruum to be used and partly upon the nature of the active constituents of the drug and the readiness with which these can be extracted. Drugs like aconite, cinchona, nux vomica, veratrum viride, and others, require to be in fine powder, while gentian, rhubarb, krameria, squill, and the like, can be readily exhausted in coarser powder. As a rule, strongly alcoholic or ethereal menstrua are used with fine powder, whereas hydro-alcoholic and aqueous menstrua are better adapted to coarser powders.

The quantity of menstruum to be used for moistening the powder also varies with different drugs; one-fourth to one-half as much menstruum as powder is generally required to thoroughly dampen it without destroying its mobility, depending likewise upon the nature of the drug and menstruum. In a few cases, where the active constituents are quickly extracted, and previous moistening might cause the powder to agglutinate, as in tincture of catechu and the official oleoresins, it is even better not to moisten the drug at all before placing it in the percolator.

The next step is the proper packing of the percolator, and upon it will largely depend the success of the process. A suitable support must be provided for the moistened powder, and for this purpose a notched cork or a tuft of absorbent cotton may be used. If the cork be chosen a layer of cotton should be placed over it to prevent the escape of powder, or if cotton alone be used, it may be slightly compressed into the neck of the percolator. Unless the quantity of drug be large, the moistened powder, after having been first passed through a coarse sieve to break up any lumps, should be transferred to the percolator *all at one time*, and then shaken down by tapping the sides of the vessel. If the drug is to be saturated with menstruum before maceration, as in the case of fluid extracts, the powder should be at once compressed, moderately or firmly as the character of the menstruum and the nature of the drug may require. As a rule, fine powders and alco-

holic menstrua demand firm packing, as also ligneous and spongy drugs under certain conditions; aqueous menstrua generally necessitate moderate compression. If the moistened drug be introduced in layers, uniform packing becomes more difficult; the lower portions of the drug should be less firmly compressed than the upper layers, because the menstruum, when it reaches them, being already charged with some soluble matter, is denser than at the top, and hence cannot penetrate a firmly packed mass as readily as would fresh menstruum. Maceration of the moistened powder prior to percolation is advantageous in many cases, as it allows the drug to swell and become more thoroughly permeated by the menstruum, and permits more satisfactory packing afterward; in some cases, where concentrated solutions are desired, maceration after saturation is positively necessary to insure good results. The packing of the moistened powder is best effected with a packing stick of suitable design, made of hard wood, of the shape of the well-known potato-masher. Next to uniformity in fineness of powder, uniformity in packing is the most important feature in percolation, so as to insure the even descent of the menstruum; if the drug is more firmly compressed on one side than on the other, the menstruum is sure to flow in the direction of least resistance, and leave a part of the mass imperfectly extracted. After the powder has been packed, a diaphragm of filtering paper or felt is laid over the surface and kept in place by means of pebbles or pieces of broken glass; this is for the purpose of preventing disturbance of the upper layer and to insure equal distribution of the liquid when the menstruum is poured on.

FIG. 105.

Glass receiving jar, graduated in U. S. fld. measure.

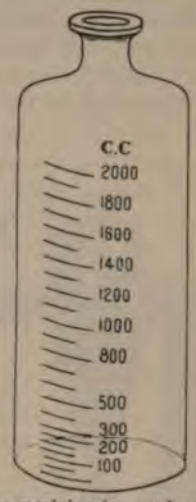
As stated in the pharmacopœial directions, a layer of menstruum must constantly be maintained above the powder, in order to prevent the access of air to its interstices. Every percolator should be provided with a cover, which may be either of glass or sheet-rubber, to avoid loss of or change in the menstruum.

The simplest arrangement for controlling the rate of flow of the percolate is by means of a rubber tube, as specified in the official directions, and this device can be attached to nearly every form of percolator known. As the rate of flow from the tube will be proportionate to the difference in height between the liquid in the percolator and the point to which the tube is raised on the outside, it is evident that its control is within easy reach and may be varied from a constant stream to five drops per minute. The rapidity with which the percolate shall be allowed to pass will vary with the object in view and the ease with which the active principles enter into solution; for tinctures, the average rate may be stated to be 15 to 20

drops per minute, while the percolate in the case of fluid extracts should not be allowed to flow faster than 5 or 10 drops per minute.

The complete exhaustion of a drug can only be judged by the physical properties of the last portions of the percolate; hence a thorough knowledge of the valuable constituents sought to be extracted is essential; absence of color and odor is not always indicative of perfect exhaustion, and the sense of taste furnishes a more reliable test in the case of aconite, ginger, nux vomica, etc. Drugs like jalap and podophyllum are known to be exhausted when the percolate mixes clear with water, as this will not occur until all resin has been extracted. Cardamom, valerian, vanilla and similar aromatic drugs are judged entirely by the odor of the percolate; quassia, rhamnus and gentian, by the bitter taste; and rhatany, catechu and geranium, by the peculiar astringency of their soluble constituents.

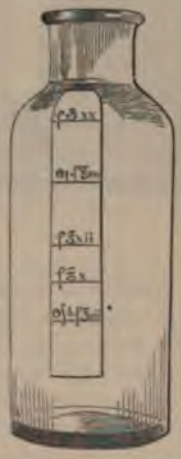
FIG. 106.



Glass receiving jar, graduated in metric fld. measure.

A considerable quantity of alcoholic menstruum is sometimes retained by the marc after exhaustion of the drug, and this may be recovered by expression or by percolation with water, either direct or after admixture of clean sawdust. Such recovered alcohol is unfit for further use until it has been purified by adding three grains of potassium permanganate to every pint, shaking the mixture occasionally during several days, and then decanting and distilling. Another plan to avoid the loss of alcohol by absorption is to employ gradually weaker menstrua, after the required quantity of original menstruum has all been added.

FIG. 107.



Graduated glass receiving jar, home-made.

Much time and annoyance may be saved by collecting the percolate in properly graduated glass jars (if the percolate is to be weighed, use tared vessels), which can be obtained from glass manufacturers in different sizes adjusted both for apothecaries' and metric fluid measure (see Figs. 105 and 106). A convenient plan also is to paste a strip of paper on a wide-mouth bottle and mark on the same with ink the different quantities of liquid measured into the bottle, as shown in Fig. 107; to protect the paper scale and render it impervious to moisture, it should be coated with some colorless varnish.

The usual method of supporting percolators is by means of the iron rings of a retort-stand, as already shown in Fig. 104; in order to protect the glass, sections of rubber tubing may be attached to the rings, forming suitable cushions or guards. A very convenient arrangement is Beck's Percolating Stand (see Fig. 108), which admits of simultaneous multiple operations and is equally well adapted for use in the store or laboratory. The stand can either be placed on the floor or be supported on two iron brackets fastened to the wall; as shown in

FIG. 108.

Beck's percolating stand.

the illustration, it can be changed by means of thumb-screws to suit various heights of bottles. The length of the base-board is 42 inches, the width 12 inches, and the extreme height of the stand 36 inches; the supports for percolators and funnels are formed by means of cross-pieces suitably hollowed out and secured by screws passing through the slot in the cross-bars.

REPERCOLATION is a process intended for the preparation of concentrated vegetable solutions with a minimum quantity of menstruum, and is confined to the manufacture of fluid extracts without heat. Dr. Squibb, who is the author of the processs, defines it to be "the successive application of the same percolating menstruum to fresh

portions of the substance to be percolated." His suggestion was based upon the observation made that a weak solution of the constituents of a drug is a better solvent for the soluble active principles of that drug than fresh menstruum. The following example will serve to illustrate the process of repercolation: 1000 Gm. of a properly powdered drug are divided into five portions of 200 Gm. each; one portion is moistened, packed, macerated, and percolated to exhaustion, the first 150 Cc. of the percolate being set aside as finished product, the remainder being collected in fractions of 200 Cc, and numbered respectively 1, 2, 3, etc., in the order in which they are collected. The second portion of the drug is moistened with No. 1 weak percolate, packed and percolated to exhaustion, the different weak percolates being used in the order in which they have been collected, followed by fresh menstruum if necessary, the first 200 Cc. of the percolate from this second portion of the drug being set aside as finished product, the remainder being again collected in fractions of 200 Cc., and numbered 1, 2, 3, etc., as before. The third, fourth, and fifth portions of the drug are treated exactly like the second portion, the first 200 Cc. of the percolate in each instance being set aside as finished product. When the fifth portion of the drug has been exhausted there will be on hand five lots of finished product—150, 200, 200, 200, and 200 Cc.; total, 950 Cc.—and besides, four or five lots of weak percolate supposed to hold in solution the soluble matter from 50 Gm.; these weak percolates, properly numbered, are set aside, to be again used in place of fresh menstruum for the next lot of the same preparation, the process henceforth being continued exactly as with the second portion of the drug mentioned before. This retention of 25 per cent. of the soluble matter of one portion of the drug in the weak percolates is based on numerous carefully conducted experiments, the results of which showed that when 100 Gm. of drug are exhausted by percolation, from 70 to 80 per cent. of the total soluble constituents present are contained in the first 75 Cc. of percolate. By some the process of repercolation is termed fractional percolation, and modifications of Dr. Squibb's method, stated above, have been suggested; in every instance, however, the same principle is kept in view—namely, the use of weak percolates in place of fresh menstruum.

CONTINUOUS PERCOLATION is a name sometimes applied to a process of extraction which involves the exhaustion of a drug with a limited quantity of menstruum, by repeatedly vaporizing and condensing the fluid in a specially constructed apparatus, so arranged that the extracted soluble matter remains in the receiving flask, while the solvent, in the form of vapor, passes upward to a reflux condenser, and thence flows back into the percolator. It is chiefly employed in the examination of vegetable drugs, with a view of determining their valuable constituents, and is particularly adapted to the manufacture of the official oleoresins. For description of the apparatus see the chapter on Oleoresins.

CHAPTER IX.

SEPARATION OF NON-VOLATILE MATTER.

THE process of separation may be applied to non-volatile or fixed as well as volatile matter; in the former case it is understood to refer to the removal of insoluble substances, sediments, etc., from fluids holding them in suspension, and also of immiscible fluids from each other. The various operations employed for the separation of solids from fluids are termed filtration, decantation, expression, clarification, and decoloration.

Filtration.

By some pharmacists filtration is considered so trivial an operation as not to merit extended consideration; but, like other simple processes, it is well deserving of study, as there is room for the exercise of intelligence and ingenuity in its many useful modifications. Filtration is usually employed when the solid matter to be removed is not present in excessive quantity, and consists in submitting the mixture to the separating action of certain media which allow the fluids to pass through but are impervious to the solid particles. Sometimes filtration is also called colation or straining; but it is understood that the process of straining differs from filtration either in the less complete removal of suspended sedimentary matter from a fluid, or in the fact that the solid particles are not in fine powder and can be easily retained by coarser media than those generally employed for filtration. Colation is a favorite mode of separation when the fluid is of a viscid character. The various filtering media employed are cotton and woollen cloth, paper made therefrom, also absorbent cotton, glass, wool, asbestos, sand, and charcoal; the clear clear liquid passing through these media is termed the filtrate.

For straining syrups, oils, and similar fluids, filter-bags of flannel or felt are admirably adapted, as they permit a rapid passage of the liquid and effectually retain all solid matter; such filter-bags are of conical shape, see Figs. 109 and 110, and are readily made, of plain or Canton flannel, by folding over a square piece in the manner indicated in Fig. 111, the line *c d* being laid over the line *c a* and united by a seam; the bag thus formed is pointed at *c* and open from *a* to *b*, the line *a c* being lapped over to form the seam. The long end projecting toward the point *b* beyond the dotted line *e f* should be removed and four loops of heavy cord or tape attached after the edge has been turned over; the loops will serve to suspend

the filter-bag properly in a square or round frame, as shown in Fig. 112. For some purposes, as the straining of dense saline solutions or

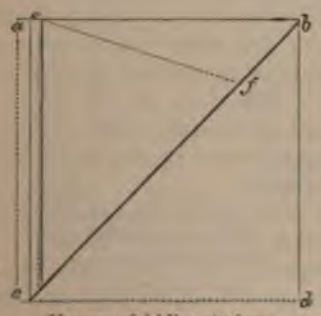
FIG. 109.

Flannel strainer.

FIG. 110.

Filter-bag.

FIG. 111.



Manner of folding strainer.

FIG. 112.

Straining bag, showing position when in use.

FIG. 113.

Frame for cloth or flannel strainers, known as "tenaculum."

the washing and draining of bulky precipitates, a square cotton cloth may be stretched over a square frame called *tenaculum*, as shown in Fig. 113; for smaller operations, such as straining infusions or decoctions, the cloth strainer may be fastened over a funnel by means of wooden pinchcocks, and when it becomes necessary to strain with expression, the ends of the strainer must be folded over and twisted in opposite directions, as shown in Fig. 114. A kind of cotton cloth

Fig. 114.

Showing the manner of folding and expressing flannel or cloth strainers.

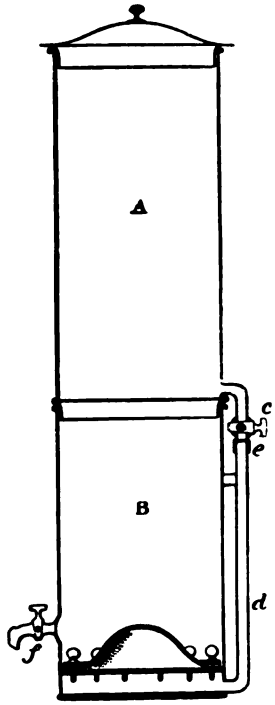
known as cheese-cloth is preferred by many for strainers, as it allows liquids to pass rapidly through it. All strainers should be well wetted just before they are used, and those containing sizing should be freed from the same by washing with hot water before they are put into use at all. For use at the dispensing counter in straining solutions, a pledget of absorbent cotton placed in the throat of a funnel will be found very convenient and serviceable; and, as nearly every solution prepared is likely to contain some specks and motes, this little operation should never be neglected.

Some years ago a very serviceable oil filter was devised by William R. Warner, which possesses the advantage of filtration under pressure, and is equally well adapted to syrups (see Fig. 115). The upper cylindrical vessel of tinned iron is twenty-two inches high and ten inches in diameter, with a flanch rim soldered on the bottom, of rather less diameter and an inch wide, so as to fit firmly into the open top of another cylindrical vessel, B, of the same diameter, eighteen inches high. The upper vessel is furnished with a lid and with an L-shaped tube and stopcock, *c*, which penetrates the side close to the bottom, and fits into another tube, *d*, at *e*, which tube opens into the lower vessel close to its base, and is further secured to B by a tubular stay. The filtering medium is a cone of hat felt, projecting upward from near the bottom of the lower vessel, and secured in place by thumb-screws passing through two tinned-iron rings and the felt, which are all properly pierced for that purpose. The stopcock, *c*, being closed, the upper vessel is fitted in its place, and the tube-joint, *e*, rendered tight by wrapping with isinglass plaster;

when this is dry, the upper vessel is filled with the liquid to be filtered, and the stopcock, *c*, opened. The filtered liquid, as it accumulates in B, should be drawn off at *f*, and if convenient the apparatus should be kept in a temperature of about 120° F., in order to facilitate the flow of the liquid.

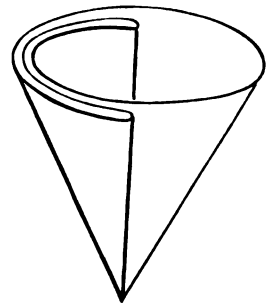
Complete separation of fine suspended matter from fluids can best be effected by means of filtration through paper; only unsized paper

FIG. 115.



Warner's oil filter.

FIG. 116.



A plain filter.

can be used, the best kind being that made from cotton and linen rags, although paper made from woollen material is tougher, and, being more porous, permits more rapid filtration. The square sheets of filtering paper, which at one time were the only style to be had, are rarely used now, since ready-cut round filters can be had of all sizes and qualities. Two kinds of paper filters are used, the *plain* and the *plaited*, the construction of which is very simple, and, when once properly understood, never forgotten. The chief advantages of plain filters are the simplicity of construction and the fact that they are admirably adapted for collecting the solid matter suspended in the fluid, which is afterward to be removed from the paper for further use; on the other hand, filtration proceeds far less rapidly in a plain than in a plaited filter, because the paper lies flat against the sides of the funnel, and the liquid passes through only at the point or apex. Plain filters are made by doubling a circular piece of filtering paper upon itself, and then folding this directly in the middle; by now opening the folds in such a manner that one sector or division shall appear on one side and three sectors on the other side, a perfect cone will be obtained, as shown in Fig. 116, which will exactly fit into a properly-shaped funnel.

The waste of paper which is caused by this method of folding a plain filter, where three thicknesses of paper are found on one side of the filter and but one thickness on the other side, may be avoided

FIG. 117.

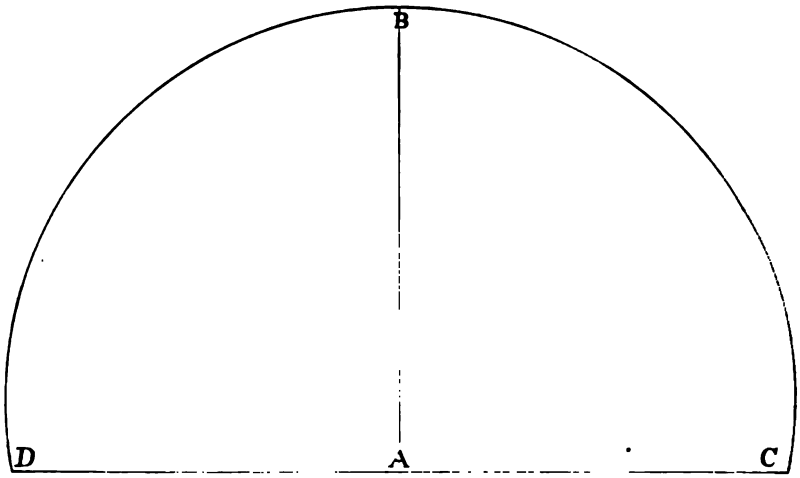
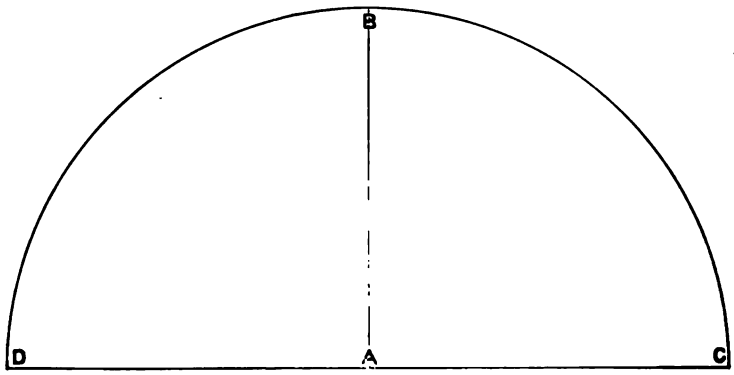


Diagram for making an economical plain filter, according to E. Classen's directions.

by following the suggestions of Edo Classen, which are as follows: To make a plain filter, of single thickness, which will fit a funnel having an angle of 60°, use a piece of filter-paper in the shape of

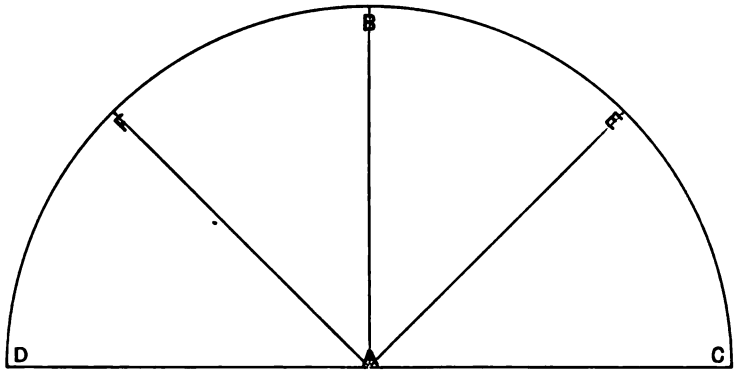
FIG. 118.



a semi-ellipse, as shown in Fig. 117, the line A B being one-fifth longer than the lines A C or A D. Fold the paper in the centre so that one-half exactly covers the other; next fold the short straight

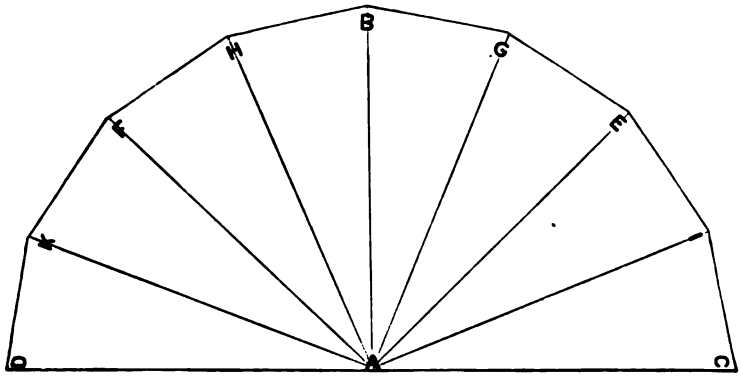
side over, so that both straight sides shall be of the same length. Additional security against leakage will be obtained if the strip last folded is again folded back upon itself, preferably toward the inside.

FIG. 119.



In order to strengthen the weakest point of the cone, a smaller round filter may be placed on the outside of the larger filter and folded with the same, or one plain filter may be placed inside of another, so that even thicknesses of paper shall be on all sides.

FIG. 120.



The construction of a plaited filter is more readily demonstrated than explained; the simplest plan is to proceed as follows: Fold a circular piece of filtering paper twice, after the manner directed above for a plain filter; this gives creases A B, A C, and A D. (See Fig. 118.)

Next fold the crease A C over on A B, and the crease A D over on A B; this causes the creases A E and A F. (See Fig. 119.)

Now fold the crease A C over on A F, the crease A D over on A E, the crease A C over on A E, and the crease A D over on A F; this causes the creases A G, A H, A I, and A K. (See Fig. 120.)

The semicircle is now divided into eight sectors, all creases being in the same direction; to complete the filter it is necessary to divide each sector into two by making a crease in a direction opposite to those already made—thus: (See Fig. 121.)

FIG. 121.

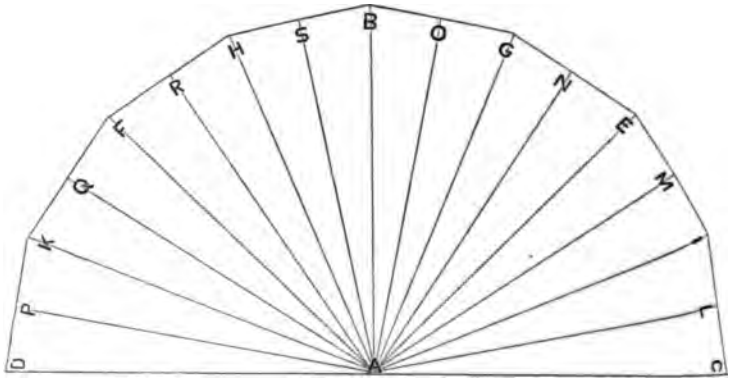


Diagram showing the creases of a plaited filter.

Fold the triangle, A C I, back upon itself; this causes the crease, A L.
" " " A I E, " " " " " " " A M.
" " " A E G, " " " " " " " A N.
" " " A G B, " " " " " " " A O.
" " " A D K, " " " " " " " A P.
" " " A K F, " " " " " " " A Q.
" " " A F H, " " " " " " " A R.
" " " A H B, " " " " " " " A S.

FIG. 122.

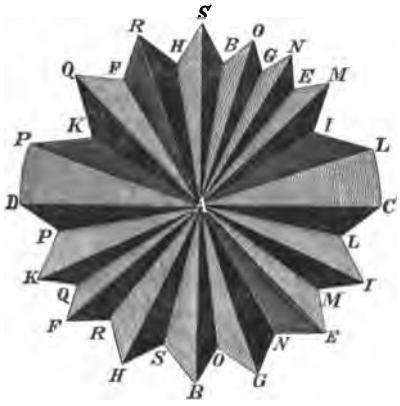
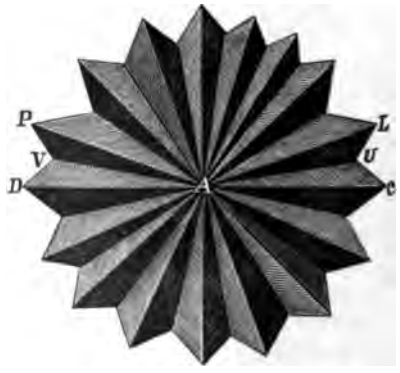


FIG. 123.



If the filter now be opened, it will be found divided into 32 sectors, two of which, A C L and A D P, opposite each other, show both edges pointing in the same direction (see Fig. 122); to prevent these two sectors from lying flat against the glass when the filter is placed in the funnel, they should be again divided by placing the index finger in the centre and bringing the edges up with the thumb and second finger, thus forming two new creases inward, A U and A V. (See Fig. 123.) In plaiting a filter, care must be observed that the creases be not pressed too firmly down to the very point, as this has a tendency to rupture the paper, or at least, to materially weaken it. The plaited filter, when completed and ready for use, is divided into 34 sectors, and appears as shown in Fig. 124.

FIG. 124.

A complete plaited filter.

FIG. 125.

A properly shaped glass funnel.

The points of paper filters may be toughened or strengthened by dipping them into strong nitric acid of 1.42 sp. gr, and then washing well with water to remove excess of acid; while a similar treatment with sulphuric acid converts unsized paper into parchment paper, which is impervious to water. Nitric acid simply toughens the paper, but in no wise interferes with the absorption and passage of fluids through it, though its power of resistance is increased tenfold by this treatment.

When the object of filtration is to obtain a clear fluid irrespective of the solid matter removed, a plaited filter is always to be preferred to the plain one, as it exposes the entire surface of the paper to the liquid and allows the latter to pass through very rapidly.

Glass, porcelain, or metallic funnels, intended as supports for paper filters, should be of the shape shown in Fig. 125, having

straight sides at an angle of 60° to each other, and the end of the tube being cut off obliquely, so as to compel the liquid to flow from one point only; when used over a jar or beaker it is well to place the lower end of the funnel in contact with the side of the vessel, thus preventing any annoyance from splashing of the liquid. In order to provide for the necessary escape of air from the receiving vessel, whenever a funnel is placed in a bottle a piece of twine or a strip of paper should be placed between the neck of the bottle and the tube of the funnel, the end of which should invariably project below the neck of the bottle.

When a paper filter is placed in a funnel, its upper edges should never quite reach to the rim of the funnel (better one-half inch below), so as to allow the funnel to be covered with glass or sheet-rubber, for the purpose of keeping out dust and preventing evaporation; besides, if the filter projects beyond the funnel, considerable liquid will be drawn to the upper edges, owing to the capillarity of the paper, and evaporated, thus entailing loss. In pouring a liquid into a filter, it should never be allowed to fall in a stream upon the apex or point, which is likely to break from the sudden force, but should be directed against the side by means of a guiding-rod, as shown in Figs. 126 and 127.

Fig. 126. Fig. 127.

Manner of pouring liquids into a filter with the aid of a guiding-rod.

To insure a continuous supply of liquid to the filter, a bottle containing the fluid may be inverted over the funnel, in the manner shown in Fig. 104, for supplying menstruum to a percolator.

For filtration of very volatile liquids, a glass tube, bent as in Fig. 128, may be placed under the filter against the side of the funnel; the twisted end will prevent the tube from slipping down,

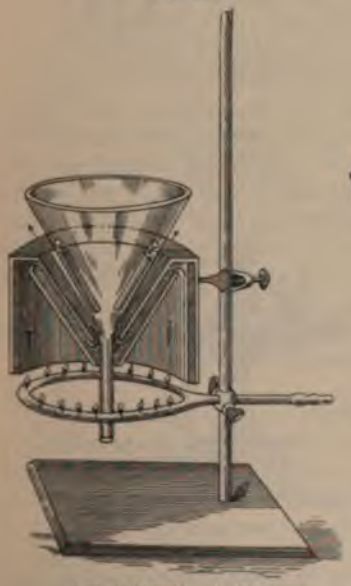
and air from the receiving-bottle can readily pass up through the tube, which should reach a little above the paper filter. The funnel, which should pass air-tight through a cork, must also be closed hermetically at the top.

FIG. 128.

Glass tube with twisted end.

Occasionally the filtration of substances which are not fluid at ordinary temperature becomes necessary, such as mutton suet, wax, petrolatum, ointments, etc.; this can be effected either by means of a hot-air funnel or a water-bath funnel. When hot air is to be used, the funnel containing a filter is suspended by means of porcelain strips, in a heavy tin jacket, which is surrounded by a copper cylinder, and heat is supplied from a circular low-power burner, as shown in Fig. 129, the heated air continually circulating around the funnel. The water-bath funnel consists of a glass funnel surrounded by a double tin or copper jacket, as shown in Fig. 130; the opening, *a*, at the top of the jacket is for the purpose of introducing hot water, and the projecting tube, *c*, near the bottom, for keeping up the heat of the water by means of a spirit lamp or gas jet. The projecting rim, *e*, is intended to prevent any water, running over

FIG. 129.



Hot-air funnel. (L. MEYER.)

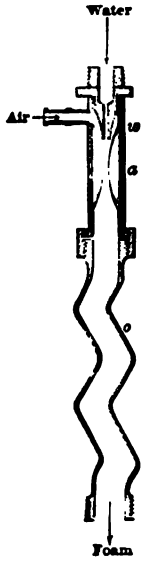
FIG. 130.

Sectional view of hot-water funnel with cover.

at *a*, from entering the bottle or vessel, in the mouth of which the neck of the funnel may be placed. The substance to be filtered

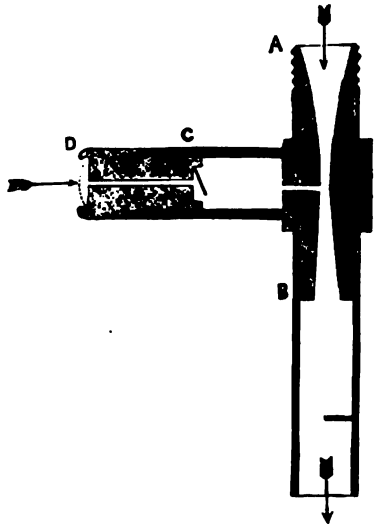
should first be completely melted and then poured into the filter contained in the previously heated funnel, which must be kept covered to avoid loss of heat.

FIG. 131.



Richard's filter pump.

FIG. 132.

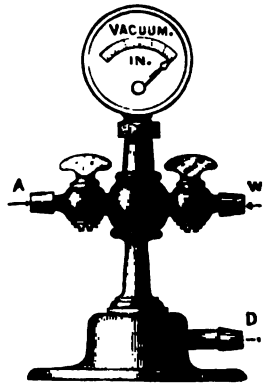


Chapman's filter pump.

FIG. 133.

Geissler's glass filter pump.

FIG. 134.



Portable filter pump, with manometer.

The rate of filtration of a liquid can be greatly increased by exhausting the air from the funnel-tube and receiving-bottle, thereby increasing the atmospheric pressure above the liquid; the necessity for this operation occurs more frequently in the analyst's laboratory than with pharmacists, yet an acquaintance with the apparatus employed

is desirable. The exhaustion of the air is effected by means of an aspirator connected with a water supply and with the receiving-bottle by rubber tubing. Figs. 131, 132, 133, and 134, represent different styles of filter pumps; as seen in two of the illustrations, suction of air is produced by forcing water, under pressure, through a contracted space which communicates with the air to be aspirated. The internal construction of the pump shown in Fig. 134 is similar to that of the other two, but the water which enters at W is discharged at D on the side; hence this apparatus can be used at any desired point, being connected by means of tubing with the water supply and sink: with air-tight connections a nearly absolute vacuum can be obtained, as may be seen from the indications of the manometer attached to the top of the pump. Whenever filter pumps are used, the pressure on the liquid filtering becomes so great as to endanger the safety of the filter point; an extra support is therefore provided in the shape of a finely perforated platinum cone set in the throat of the funnel in which the paper cone is placed.

When an aspirator or filter pump is used in connection with water drawn from the city supply, a very annoying accident sometimes happens when the water pressure is suddenly reduced, or when the pump is cut off; namely, that a portion of water is drawn up into the vessel from which the air is being aspirated; this can be guarded against either by interposing another vessel between the pump and the aspirated vessel, or by introducing into the tube connecting the pump and vessel a safety-valve as designed by Wislicenus, and shown in Fig. 135. It consists of two glass tubes of peculiar shape fitting snugly into each other at *f*, the bulb being well coated with resin cerate; the tube B is fitted into the rubber tube attached to the pump, and the tube A into the tube attached to the vessel. At *r* a solid soft-rubber ring rests in the upper part of the tube B, and closes the same air-tight as soon as suction is established; while at *o* there is an opening in the closed end of the tube A, which is covered with thin sheet-rubber, as shown in Fig. 135. As soon as the suction of air ceases from any cause, the opening at *o* is tightly closed by the rubber, and no water can enter. If any water is drawn up into B, it is emptied by withdrawing the tube A, the rubber ring becoming loose.

For rarefying the air under filters when water pressure is not available, a simpler contrivance may be resorted to, as shown in Fig. 136: the water flowing from the upper to the lower bottle withdraws air from the receiving-flask, and by simply changing the bottles when the upper one becomes empty, the operation may be continued for any length of time, the air-tube being closed by means of a pinchcock, while the bottles are being changed. Ordinary five-gallon castor-oil cans may be conveniently used in place of bottles.

The turbidity of some liquids is caused by suspension of matter in so finely divided a form that its removal cannot be effected by the

ordinary methods of filtration, and recourse must be had to the interposition of some other substance to render the liquid perfectly transparent and clear; in such cases paper pulp, calcium phosphate, and

FIG. 135.

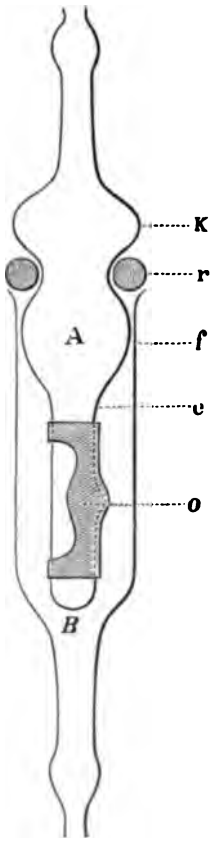


FIG. 136.

FIG. 135.—Wislicenus safety-valve.

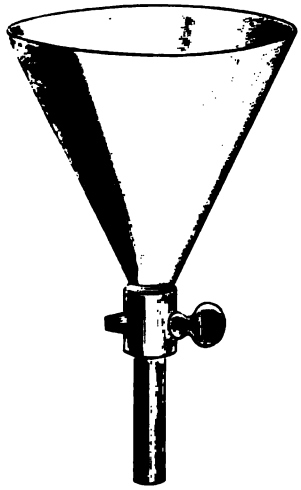
FIG. 136.—Filtering apparatus. *a* and *b* are two large bottles connected, as indicated in the drawing, by a narrow india-rubber tube with thick walls. The upper bottle should be placed as high as possible. *c* is a bottle into which the filtrate is to pass. The interior of this is in connection with *a* by a thick-walled tube, *d*. Into the stopper of *c* the funnel *e* is fixed, and at its apex lies a small perforated platinum cone, *f*, which supports the apex of the filter when the interior of *c* is partially exhausted by the discharge of the water in *a* into *b*.

purified talcum form excellent filtering media. Paper pulp is readily prepared from scraps of filtering paper by treating them with hot water in a mortar or with active agitation in a bottle. When the paper has become thoroughly pulped, the excessive moisture may be removed by expression in a clean cloth, after which the pulp may be added to the liquid to be filtered and thoroughly incorporated by

agitation. The finely divided paper pulp forms a layer on the surface of the filter, which effectually prevents the passage of minute particles of insoluble matter by absorbing these into its own fibre. For acid liquids, finely shredded asbestos is preferable.

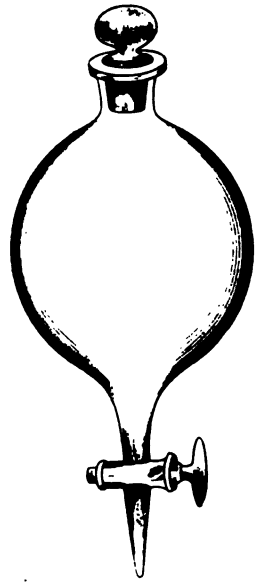
Immiscible liquids can be conveniently separated from each other by pouring the mixture into specially constructed apparatus known as separators or separatory funnels (see Figs. 137 and 138), and after

FIG. 137.



Glass separator. (Funnel shape.)

FIG. 138.



Glass separator. (Globe shape.)

the liquids have separated into distinct layers by reason of their different specific gravities, withdrawing the lower liquid by carefully opening the stopcock in the tube and allowing it to flow into a suitable receiving vessel.

Decantation.

Decantation, or the process of pouring a fluid gently from one vessel to another, is employed in pharmacy more particularly in connection with the washing of precipitates; sometimes it is resorted to for the separation of immiscible liquids, but separation in such a case can never be so complete as by the method explained above.

All precipitates when freshly obtained by double decomposition of two soluble substances, are more or less contaminated with a solution of the other newly-formed salt; to remove such impurities the process of washing, which consists in treating the precipitate repeatedly with

fresh portions of water, is employed. Thus, when solutions of lead nitrate and potassium iodide are mixed, the newly-formed lead iodide is deposited, while potassium nitrate remains in solution, and must be removed before the precipitate can be dried. The thorough washing of precipitates is a very important operation, which may be performed by continued treatment with water on filters and cloth strainers, or by allowing the liquid in which the precipitate was formed to settle completely in suitable vessels, decanting the clear supernatant fluid, adding successive portions of fresh water, and again decanting after each settlement: it is essential that the fresh water and precipitate be well mixed by stirring or agitation after each addition.

The decantation of a fluid is not always so simple an operation as it may seem: the shape and size of the vessel from which the liquid

Fig. 139

Decantation with aid of a glass rod.

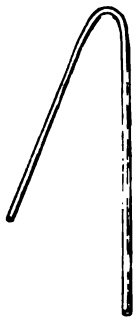
is to be poured, the nature of the liquid and the height to which it fills the vessel, all influence the flow of the liquid. When the fluid to be decanted is water or an aqueous solution, and the vessel not very large, either with or without a lip, the simplest plan is to transfer the liquid with the aid of a glass rod, as shown in Fig. 139. The guiding-rod prevents the splitting of the current of the liquid, to which is due the well-known phenomenon of liquids running back on the sides of the vessel from which they are poured. When the vessel from which the liquid is to be poured is too large or too full of liquid to admit of decantation with the aid of a glass rod, the liquid may be made to flow in a somewhat contracted but solid stream by greasing the rim of the vessel with a little resin cerate, which prevents adhesion of the liquid to the glass and enables the force of cohesion to keep the particles of liquid united; Fig. 140 illustrates the operation.

Sometimes an instrument called a *siphon* is employed to draw off the supernatant liquid from a precipitate, the method being particularly desirable if the precipitate is light and easily disturbed by handling the vessel; the simple construction of a siphon is shown in Figs. 141 and 142. The two limbs of the glass tube are of unequal length, the shorter one being immersed in the liquid; it is manifest that if the air be entirely withdrawn from the tube by suction, the liquid will rise and fill the tube, owing to the pressure of the atmosphere on the surface of the liquid. The flow of the liquid, having been started, will continue by reason of its downward tendency or gravitation aided by atmospheric pressure, until it falls below the mouth of the shorter limb, or until that in the receiving vessel rises to the level of that in the vessel from which it flows. A plain rubber tube can often be used with advantage as a siphon, remembering that the end of the tubing out of the liquid should always reach lower than that in the liquid, so as to insure a continuous flow.

FIG. 140.

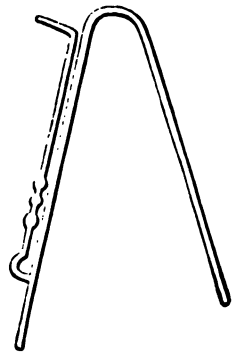
Decantation with aid of a greased rim.

FIG. 141.



Plain siphon.

FIG. 142.



Glass siphon with lateral suction tube.

Clarification.

Clarification is a process of separation designed to render cloudy or turbid liquid transparent by means other than those thus far con-

sidered; it is generally effected through the agency of heat; in every instance, however, the separated disturbing element must subsequently be removed by filtration or decantation. The viscid character of some liquids renders the various methods of filtration impracticable; whereas the mere application of heat, by increasing their fluidity, enables the suspended particles of solid matter to separate spontaneously, some rising to the surface while others sink to the bottom; if the liquid be allowed to remain at perfect rest while separation is going on, the lighter particles will form a layer, which can often be completely removed with the aid of a skimmer, while the heavy sedimentary matter is readily retained on a cloth strainer. Honey and balsam of fir may be treated in this manner. Saline solutions concentrated for the purpose of crystallization are frequently contaminated with dust and other foreign matter which passes freely through cloth and paper filters; they may be readily clarified by adding paper-pulp (see page 144), which effectually removes the fine particles of dirt from the boiling liquid, by enveloping them in its own fibre and retaining them on the strainer.

Other substances added to turbid liquids in order to effect clarification are egg-albumen, gelatin, and milk. White of egg, or albumen, possesses the property of coagulating or solidifying when heated to about 80° C. (176° F.), therefore, when they are added to liquids and then heated, any solid matter impairing the transparency of the liquid will be enclosed in the coagulum formed, and can then be removed by straining; some vegetable solutions prepared with cold aqueous menstrua contain albuminous matter originally present in the drug, which, upon heating to the boiling-point, is coagulated, and is thus gotten rid of, as in the case of extract of gentian. Albumen is preferably mixed with a little water before adding it to the liquid to be clarified, and then thoroughly incorporated with it before heating. Since albumen forms insoluble compounds with some plant constituents, it must be judiciously employed, lest the active principles contained in a liquid be removed by it. When the turbidity of a liquid is due to tannin, gelatin is generally preferred as a clarifying agent; it is used like albumen, and forms insoluble tannate of gelatin, or leather. Milk is especially adapted to clarifying acid liquids, as the casein of the milk is coagulated by the acid, and thus the impurities are removed by becoming enveloped in the coagulum.

Clarification of liquids may also be effected by subsidence and fermentation; the former is often applied to fixed oils, which are allowed to remain undisturbed in tightly closed containers for some time, so that albuminous matter derived from the seed may gradually separate and settle to the bottom. Fruit juices, as a rule, contain certain principles which tend to render them cloudy and unsightly, but which can be removed by fermentation at a moderate temperature, about 20° C. (68° F.); the matter thus separated settles to the bottom

and the clear liquid may be drawn off by means of a siphon or otherwise.

Decoloration.

Decoloration, as the name indicates, is a process for the removal of color from liquids, and is practised on a large scale in sugar refineries. For pharmaceutical purposes it is chiefly confined to solutions of organic acids, alkalies, and neutral principles. The most effective decolorizing agent is animal charcoal, made either from bone or blood; ordinary bone-black requires purification by means of hot hydrochloric acid, whereby certain lime-salts are removed. Animal charcoal is preferably used in a granular condition, and its utility as a decolorizer depends upon its porosity; unfortunately, charcoal also absorbs other matters held in solution besides color, and this may occasion loss of valuable constituents unless the charcoal is subsequently washed with fresh menstrum. The usual method of employing animal charcoal is either by digesting it with the liquid to be decolorized, or by allowing the latter to percolate slowly through a column of the charcoal; in the former case the liquid requires subsequent filtration.

Expression.

Expression is a process of separation which requires the exercise of more or less force, since it is employed in those cases where the amount of liquid is small compared with the quantity of solid matter to be removed; as, for instance, in the preparation of fruit juices, the expression of macerated drugs, or the recovery of menstruum that may have been retained by the marc in percolation when water fails to force it through. For the purposes of the pharmacist, the tincture press, Fig. 143, and the Enterprise Press, Fig. 144, will be found very serviceable; in the former the substance to be expressed, having been put into a suitable canvas or press-cloth bag, is placed on a perforated disk in a porcelain-lined iron cylinder, pressure being produced by means of a lever-screw bearing upon a plate on top of the bag. The expressed liquid flows out through the lip attached to the cylinder. The Enterprise Press is operated without the use of press-cloths, the material to be ex-

FIG. 143.

Tincture press (vertical).

pressed being fed directly into the hopper communicating with a tapering cylinder containing a large screw, the thread of which gradually diminishes in size toward the smaller end; the cylinder is provided with a perforated plate in the bottom, and the material is compressed by means of the tapering screw, which is turned with a

FIG. 144.

Enterprise press (horizontal).

crank. The dry residue is discharged through an opening in the small end of the cylinder, and the liquid expressed flows out through the perforated plate.

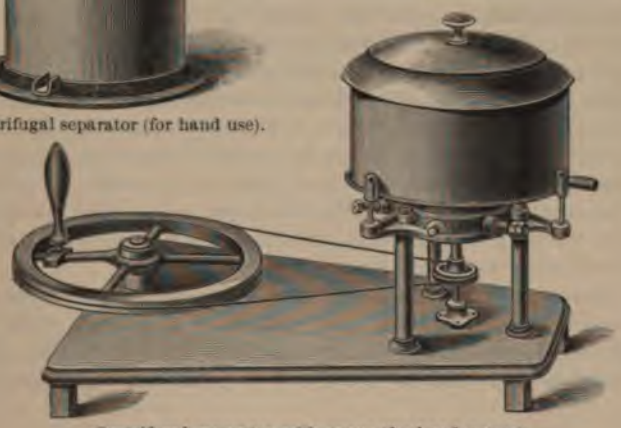
Another method of separation is that effected by means of centrifugal machines, which are extensively employed in manufacturing establishments for washing and drying crystals as well as for the rapid withdrawal of moisture in the drying of certain precipitates and fabrics. The apparatus used consists of a metal drum or cylinder having a solid bottom but open at the top, and provided with perforated sides, which revolves on its own axis inside of a larger stationary cylinder supplied with a cover to keep out dust, and an outlet tube at the bottom, through which the liquid coming from the inner cylinder is allowed to flow out; sometimes the perforated sides of the inner cylinder are covered with bolting-cloth, according to the substance to be operated upon, and the rotary motion is imparted to the cylinder from below by means of steam power. The value of centrifugal machines depends upon the velocity with which the material to be centrifugalized is hurled around and against the perforated sides, the revolutions usually running as high as 2000 or 3000 and even more per minute; the strong draft of air created between the walls of the inner and outer cylinders by such rapid revolution effects drying of the material more thoroughly than is possible by expression or other means. The use of centrifugal machines is based on the well-known laws of motion and inertia, according to which a body put in motion continues in a straight line unless turned from its

path by some external force, and thus liquids can readily be separated from solids when a mixture of the two is dashed against a finely-perforated surface. In sugar refineries, centrifugalizing is the only suitable method known for separating the granulated sugar from the viscid mother liquor or molasses. For special use in the pharmacist's laboratory, small centrifugal machines, to be operated by hand, have been devised; the outer cylinder is usually made of enamelled iron while the inner perforated cylinder is made of porcelain;

FIG. 145.

Centrifugal separator (for hand use).

FIG. 146.



Centrifugal separator with cover (for hand power).

those in which motion is supplied from above are frequently provided with a cover for the inner cylinder, while in those operated from below a cover is fitted to the outer cylinder. In Figs. 145 and 146 are shown two styles of hand-power machines.

Dialysis.

Dialysis is a process of separation which differs entirely from those considered thus far, in not aiming at the removal of insoluble matter suspended in a liquid, but at bringing about a separation between solvents and matter held by them in solution; also between different kinds of matter held in solution by the same solvent. It is a practical application of the principle of osmosis, and is due solely to surface action and the difference in diffusibility of various substances. The word dialysis is derived from the Greek verb διαλύειν, to *part*

asunder, to *loose one from another*, and was applied by Prof. Graham, of England, to the method of separation discovered by him in 1861. The process consists in placing a solution of the substances to be separated on a porous diaphragm and suspending this in pure water; osmosis is established, and certain substances will pass through the diaphragm into solution in the water, while others will remain on the diaphragm, the rapidity of diffusion being in proportion to the strength of the solution and increasing with the rise in temperature. Prof. Graham discovered that crystallizable substances passed through the diaphragm freely, while amorphous bodies, such as gums, starch, gelatin, etc., either did not diffuse at all, or only very slowly; he applied the name *crystalloid* (resembling crystals) to all substances thus capable of diffusion through a septum, and the name *colloid* (resembling glue or jelly) to those substances remaining on the diaphragm. All colloids are amorphous or non-crystallizable, but all crystalloids are not necessarily capable of crytallization, as, for instance, hydrochloric acid, the most highly diffusible body, and many others. By means of dialysis, sugar can be readily separated from gum or starch, pepsin from peptones, iron salts from iron oxide, etc. Thus the process has become most valuable to manufacturers, whilst the analyst often finds dialysis the only means for determining the presence of certain substances in complex vegetable solutions, as, for instance, arsenous acid, corrosive mercuric chloride, or potassium iodide in compound sarsaparilla mixtures and other proprietary medicines, where the dark color and complex nature of the solution preclude all other methods of separation.

The apparatus used for dialysis is of very simple construction, as shown in Figs. 147 and 148. It consists of a circular glass vessel, with flat bottom and of convenient size, also another smaller circular but bottomless vessel of hard rubber or glass, having a projecting

Fig. 147.

Fig. 148.

Glass dialysers.

rim, over which is stretched a piece of bladder, parchment, or parchment paper (see page 139). The latter constitutes the dialyser proper, and into it is poured the solution to be dialysed, to the depth of about one-half or three-quarters of an inch, after which it is floated in distilled water contained in the other larger vessel. In Fig. 148 the glass dialyser is provided at the top with a broad rim which rests upon the edge of the outer vessel, and thus serves as a cover to protect the water against dust, etc. In place of the foregoing convenient appa-

ratus, an ordinary clean hog or beef bladder may be used; the same should be three-fourths filled with the solution, and then suspended in a large vessel of water.

Diffusion in a dialyser will not take place unless the porous membrane or septum is in contact with water, and, moreover, its limit will be reached when the water on the outside becomes charged with such a quantity of crystalloids as to render the strength of the solution identical with that in the dialyser; hence it is necessary that the quantity of water in the outer vessel be much greater than that of the liquid in the dialyser, and that it be renewed from time to time. The crystalloids from a 10 per cent. solution of sugar, salt, or hydrochloric acid will readily diffuse through a septum if the latter is placed in contact with water, but no diffusion whatever will take place if the dialyser be floated in a 10 per cent. solution of the same substances. While the rate of diffusion varies greatly for different substances, it was found by Graham to be uniform for isomorphous bodies; that is, those having exactly the same crytalline form.

The colloidal residue remaining on the diaphragm is termed the *dialysate*, while the solution of the crystalloids that have passed through the membrane is known as the *diffusate*.

CHAPTER X.

SEPARATION OF VOLATILE MATTER.

ADVANTAGE may be taken of the volatility of some substances for the purpose of separation, and by their vaporization, either of the following objects may be attained:

1. The separation of a volatile liquid from a solid, with a view of retaining the solid substance, or of one liquid from another, to obtain the less volatile; in such cases the process is termed *evaporation*.

2. When the separation of liquid and solid substances, by means of evaporation, is carried to complete dryness, the process is more particularly designated as *desiccation* or *exsiccation*.

3. The separation of a volatile liquid from either a less volatile liquid or a solid, in order to obtain and preserve the volatilized liquid for future use; the process is then known as *distillation*.

4. The separation of a volatile solid from either a liquid or a solid which is more fixed, the object sought being the volatilized solid body; this process is termed *sublimation*.

Evaporation.

In the practice of pharmacy, evaporation is extensively resorted to for the concentration of vegetable and saline solutions, the latter with a special view to subsequent crystallization, and the laws which control the process should be well understood. Evaporation may be divided into four kinds; namely, evaporation over a naked fire, on a water-bath or steam-bath, in a vacuum apparatus, and spontaneous evaporation. Evaporation over a naked fire is effected by the direct radiation of heat from a fire, on the bottom of an uncovered dish or pan, and is available when the substance in solution is not injured by direct heat or high temperature; it is usually employed for the concentration of saline solutions for crystallization, but only when the liquid to be vaporized is water. When evaporation at temperatures below that of boiling water is desired, the low-power burner shown on page 73, may be used with advantage.

Evaporation on a water- or steam-bath is the method most frequently resorted to; the latter can also be employed for rapid concentration of solutions at a high temperature, without the danger of injury from direct heat of the fire. Evaporation at temperatures below 100° C. (212° F.) is effected on a water-bath, and is confined to the surface of the liquid; this is the method chosen for the concentration of vegetable and other solutions liable to be injured by

heat at or above that of boiling water and when more volatile solvents than water are present. Whenever a liquid is to be evaporated at a temperature below its boiling-point, rapidity of evaporation will depend upon the extent of surface exposed to the air, since the formation of vapor takes place only at the surface; hence broad shallow vessels are to be preferred. During the boiling of liquids the rate of evaporation depends (the source of heat being constant) entirely upon the extent of surface to which heat is applied, since the more numerous the points of contact of the vessel with the source of heat the more rapid must be the formation of vapor, and ebullition is but the phenomenon of the rapid disengagement of vapor from the interior of a liquid.

Evaporation *in vacuo*, being conducted under greatly reduced pressure, is admirably adapted to the concentration of liquids holding vegetable matter in solution, but is employed only in large manufacturing establishments, owing to the complicated and expensive apparatus necessary for the operation; the process insures rapid evaporation at a low temperature, without the possibility of injury from contact with the air. In sugar refineries weak saccharine solutions are rapidly concentrated in vacuum pans to avoid coloration and inversion of the sugar. For the preparation of fluid and solid extracts, evaporation in a vacuum apparatus offers advantages not obtainable by any other method, as a low temperature and complete exclusion of air insure the retention of soluble matter in its original form as extracted from the drug. The vacuum apparatus consists of an air-tight boiler connected with a steam-bath and an air-pump operated by machinery, for exhausting the air and vapor.

Spontaneous evaporation proceeds naturally, without the use of external force, and consists in allowing vaporization to take place at the ordinary temperature. It is due to diffusion of the vapor of the liquid into the surrounding atmosphere, and its rapidity depends upon the dryness and temperature of the air; the most effectual means of promoting it, therefore, is to allow a current of warm, dry air to pass over the surface of the evaporating liquid, as this will remove the superincumbent air as soon as diffusion into it has taken place.

The most desirable evaporating dishes for general use are those known as Royal Berlin porcelain ware (see Fig. 149); they resist sudden changes in temperature better than other earthen vessels, and possess the great advantage of not being permeable by colored fluids. When used over direct fire, a piece of wire gauze should be interposed between the flame and the dish, so as to distribute the heat more uniformly over the bottom of the vessel and prevent the flame from striking any particular point. As glass and porcelain vessels are liable to crack when suddenly brought in contact with a cold surface after having been heated, it will prove economical to

FIG. 149.

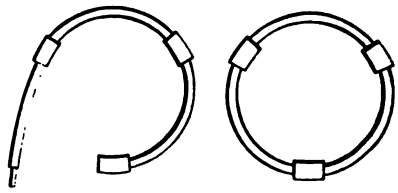
Royal Berlin porcelain dish.

place them on straw rings or rubber grommets (see Figs. 150 and 151), when hot; these also serve admirably as supports to prevent

FIG. 150.

Straw ring for supporting dishes and flasks.

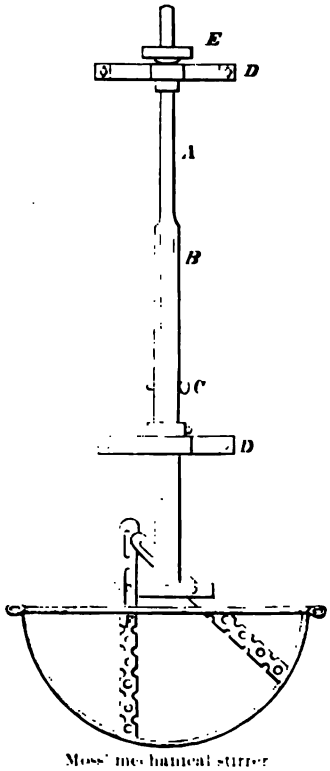
FIG. 151.



Grommets.

tilting of round-bottom dishes and flasks. Grommets are easily made by forming rubber tubing into a circle and uniting the ends by means of a wooden plug; three short pieces of similar tubing of larger size are then placed one over the joint and the others at equal distances apart, which arrangement permits a circulation of air around the bottom of the vessel. Enamelled cast-iron dishes are extensively used, but, owing to the non-uniform expansion and contraction of the metal and enamel, the latter is apt to crack and chip off, unless heat be very carefully applied; the so-called "agate ware" dishes are better, being made of sheet-iron and then enamelled. For neutral liquids, well-tinned copper pans may be employed, while for the evaporation of solutions of caustic soda or potassa, silver or perfectly clean iron vessels are necessary.

FIG. 152.



Moss' mechanical stirrer.

Evaporation of liquids in open vessels is materially facilitated by keeping the liquid in motion, which, in small operations, can be readily done by stirring with a glass rod or porcelain spatula, and on a large scale by means of a mechanical stirrer operated by steam or water power. A simple form of mechanical stirrer is shown in Fig. 152; it was devised by John Moss, of England, and consists of a 1¼ inch shaft, *A*, and a hollow shaft, *B*, which readily slides over it. These shafts are fastened together at *C*,

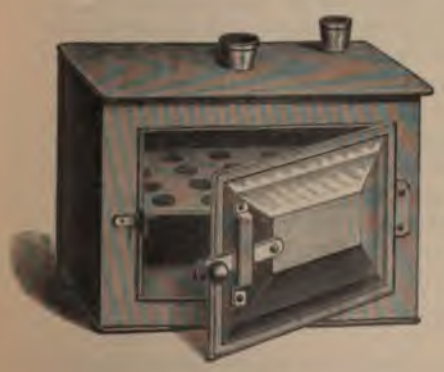
by means of a pin, and are held vertically over the centre of the evaporating pan by means of the brackets, *D*, attached to the wall. Power for turning the shaft is supplied by a band passing around the grooved pulley at *E*. To the lower end of *B* is attached a hard-wood block, on the opposite sides of which are fastened the stirring paddles, *F*, which can be set at any desired angle, by means of winged-screw bolts, as seen in the cut. The paddles, which are usually made of ash, may consist of solid blades, 2 feet long by 2½ inches wide and ⅝ inch thick, but are preferably perforated with holes not less than 1 inch in diameter, which prevent the contents of the pan from moving around as a solid mass, and insure the formation of currents of different sizes, moving at different rates of speed, whereby evaporation is greatly facilitated.

Corrosive vapors are sometimes given off during the evaporation of acid liquids; to prevent these from contaminating the atmosphere of the store or laboratory, and also to avoid saturating the air with moisture, evaporation may be conveniently conducted under a hood communicating with a flue. When evaporation is directed to be carried to a given weight, a tared dish must be used, the dish and contents being weighed from time to time until the desired weight has been reached. If evaporation is to be carried to a given volume, the simplest plan is to measure the desired volume of water into a dish standing on a level surface, then introduce into the centre of the liquid a thin stick of wood and mark the height to which the water reaches —the liquid to be evaporated must be reduced in this same dish until it stands at the point indicated by the notch on the stick.

Desiccation.

Desiccation, or exsiccation, a process of drying completely, is another method of evaporation, and is employed for driving off the

FIG. 153.



Hot-water drying oven.

FIG. 154.

Hot-air drying oven.

moisture from vegetable drugs, crystalline salts, precipitates, pills, tablets, lozenges, etc. The temperature for effecting desiccation may vary from 40° C. (104° F.) to 200° C. (392° F.), the heating being carried on either in the open air on sand-baths or in closed compartments. For small operations, and when heat not higher than 100° C. (212° F.) is required, a portable water-oven (Fig. 153) will answer admirably. This consists of a double-walled copper box containing water, which may be heated to boiling, and thus heat supplied to the interior compartment, which is provided with a perforated tray, a closely-fitting door, and an opening in the top for the escape of moisture. For temperatures above 100° C. (212° F.) a hot-air bath (Fig. 154) may be employed. This consists of a single-walled copper box through which heated air is constantly circulating, and which is provided with a thermometer through an opening in the top. In large manufacturing establishments desiccation is carried on in appropriate drying closets built of kiln-dried wood and heated by coils of steam pipe.

The term exsiccation, in pharmacy, is usually reserved for a process of evaporation in which crystalline salts are first moderately heated to efflorescence, and then with constant stirring more strongly until all water of crystallization has been expelled and the powder has ceased losing weight. Dried alum, dried sulphate of iron, and dried sulphate of copper are prepared by exsiccation. Exsiccated or anhydrous salts may be restored to their original composition by simple solution in water.

Fig. 155.

Desiccator.

Desiccator is the name applied to glass apparatus of varied construction, in which substances, after having been completely dried by heat, are allowed to cool in air which is kept entirely free from moisture by strong sulphuric acid, fused calcium chloride or freshly-burned lime, placed in the lower cup of the apparatus. Sometimes the desiccator is also used to abstract moisture from material which, owing to its volatile nature, cannot be exposed to heat without loss or injury, and since sulphuric acid and lime both have a great affinity for water, perfect desiccation can thus be effected. Fig. 155 represents one of the styles of this very useful apparatus, which is indispensable in quantitative chemical analysis.

Incineration, Calcination, and Torrefaction.

Incineration, or reduction to ash, is a process of separation applied to vegetable matter, which consists in heating it to redness in open

vessels, with full access of air, until all carbon has been consumed, or converted into carbon dioxide.

Calcination differs from incineration chiefly in being applied to mineral substances, which are heated to redness without fusion, for the purpose of expelling some volatile constituent at a high heat, as the carbonic acid from magnesium and calcium carbonates in the preparation of magnesia (calcined) and unslaked lime, or the nitric acid from mercuric and cupric nitrates in the preparation of the respective oxides.

Torrefaction, or roasting, is not so much a method of separation as one which is intended to modify the properties of substances by exposing them to dry heat to a point short of carbonization. Roasted coffee is probably the most familiar example. Thirty or forty years ago physicians used rhubarb, dried, and roasted in very coarse powder, which had thus lost its cathartic properties, but had retained its astringency.

Distillation.

Distillation differs from evaporation chiefly in the utilization of the volatilized liquid, and in order, therefore, that no loss may occur, the process must be conducted in certain closed apparatus, where the condensation of the vaporized liquid may be effected. As the application of heat to a liquid is necessary to convert it into vapor, so, inversely, the withdrawal of heat from vapor is essential to reconvert it into a liquid, and these two operations constitute the process of distillation; the necessary apparatus, then, must consist of two parts, a boiler, or vaporizer, and a condenser, to which may be attached a separate receiving vessel. The condensed vapor is called the distillate.

The rationale of the process of distillation may be explained as follows: Heat is applied to a liquid in a closed vessel, and is absorbed, which causes the liquid to change its state of aggregation to that of vapor; the vapor enters the condensing tube, where it comes in contact with the cold surfaces chilled by water on the outside; immediately it begins to part with its latent heat, transferring it to the cold surface and the water, and assumes again its original liquid form.

The temperature of steam not under pressure is 100° C. (212° F.), in addition to which it carries a latent heat of 550° C. (990° F.); if steam is condensed and the distillate collected is to have a temperature of 50° C. (122° F.), at least 600° C. (1080° F.) of heat must be given off or transferred to the water in the cooler. In other words, each liter of water converted into steam requires six liters of water at 0° C. (32° F.) to convert it back into water having a temperature of 50° C. (122° F.).

Alcoholic vapor requires only about one-half as much cold water for condensation as aqueous vapor, since its sensible heat is 78.2° C. (172.4° F.) and its latent heat only 215° C. (387° F.). The sensi-

ble heat of the vapor of official diluted alcohol is 82° C. (179.6° F.), and its latent heat about 260° C. (468° F.).

As such large quantities of water for condensing purposes are not practically available, the same object is attained—the withdrawing of the latent heat from vaporized liquids as completely as possible—by a continuous supply of cold running water. It has been frequently observed in the preparation of distilled water, that more rapid condensation takes place if the water surrounding the condenser be supplied slowly and thus allowed to become warm. The outlet, or lower end of the condensing tube, should always be kept coolest, hence cold

FIG. 156.

Simple distillation from a flask.

water must be supplied at this point and carried upward. Care must also be observed that the application of heat and refrigeration be properly adjusted, so that vapor be not generated in excess of the capacity of the condenser.

The simplest form of distillatory apparatus consists of a flask, or retort, in which the liquid to be distilled is vaporized, and a receiver

FIG. 157.

Plain retort with adapter, *a*, and receiver, *b*.

immersed in cold water, in which the vapor is condensed. When a flask is used, this is connected with the receiver by means of glass tubing, as shown in Fig. 156, while in the case of the retort, connection is made either by means of an adapter, see Fig. 157, or by in-

serting the beak of the retort directly into the receiver, as shown in Fig. 158.

To cool the vapor still more thoroughly, the beak of the retort, or the tube connecting the flask with the receiver, may be wrapped in part with cotton cloth, upon which a constant stream of cold water is allowed to trickle, the water being prevented from running into the receiver, by suspending the end of the cloth in the receptacle for

Fig. 158.

Tubulated retort and flask receiver.

waste water. Tubulated retorts have almost entirely superseded the plain variety, as they possess the advantage of being more easily filled and cleaned, and also admit of the introduction of a thermometer or safety-tube, through a cork in the tubulure. A safety-tube, Fig. 159, is often necessary in distillation from retorts or flasks, to allow the escape of large volumes of vapor accumulated and suddenly evolved, which otherwise might endanger the apparatus or cause the liquid to rise and flow over into the condensing tube. Wide-mouth, flat-bottom flasks are preferable to retorts, as they can be more readily filled, connected and cleaned, and are easily supported on a sand or water-bath.

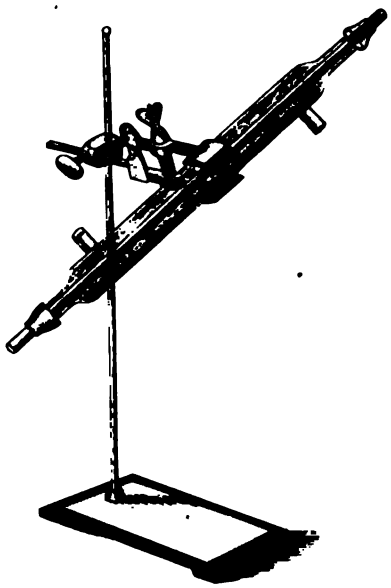
Fig. 159.

Safety-tube.

For many purposes, when the most perfect refrigeration of vapor possible is desired, the apparatus known as the Liebig condenser will be found extremely useful, its construction being such as to insure a constant supply of cold water around the condensing tube, which can be readily connected with any flask or retort by means of corks and glass tubing. Liebig's condenser consists of two tubes, one within the other; the inner always of glass, the outer of glass or metal and provided with attachments for supply and waste of water, which is made to enter near the lower end and to traverse the whole length of the outer tube before it is discharged at the upper end; therefore, as the vapor passes downward in the

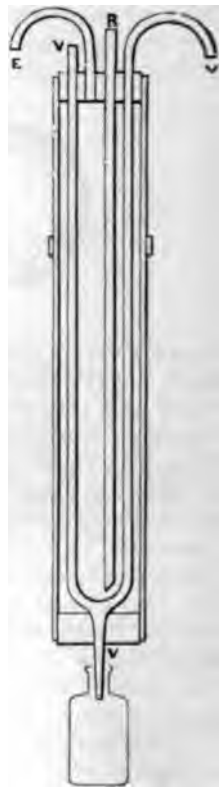
inner tube it is continually cooled, and thus perfect condensation effected before it reaches the receiving vessel. Fig. 160 shows an all-glass Liebig condenser attachable to any filtering stand and capable of being set at any angle or height, by means of the clamp support, to suit the position of the flask or retort with which it is to be connected.

FIG. 160.



All-glass Liebig condenser, with adjustable clamp.

FIG. 161.

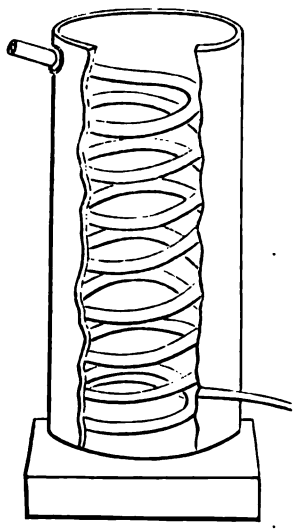


Squibb's upright condenser.

In order to economize space on the laboratory table, Dr. Squibb has devised an upright condenser, also made of glass, which can be attached, like the preceding one, to a stand; it is very effective, and differs from the Liebig condenser in having the condensing tube doubled like a U, as shown in Fig. 161. The outer lines represent the water-case tube, V V the vapor tube of U-shape with a small opening at the lower end, from which the condensed liquid escapes to a proper recipient, while any uncondensed vapor passes to the other leg of the tube, is there condensed, and flows downward to the outlet. R is the tube supplying cold water to the lower end of the water case, which rises and finally flows out through E.

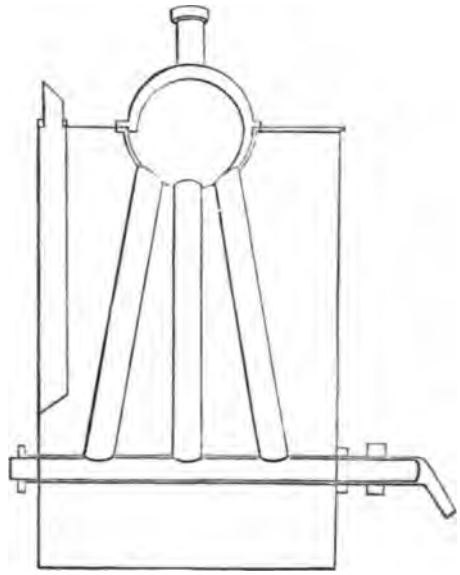
For large operations, condensation of vapor is usually effected in a metal or stoneware tube bent in the form of a spiral, and known as a *condensing worm*, see Fig. 162, inclosed in a metal or wooden case, which is kept supplied with a constant stream of cold water. On account of the difficulty encountered in cleaning the worm, other arrangements have been suggested, some of which are extensively employed in Europe. Fig. 163 represents the *Beindorf condenser*, in which the vapor is made to pass through three straight tubes, con-

FIG. 162.



Worm condenser.

FIG. 163.



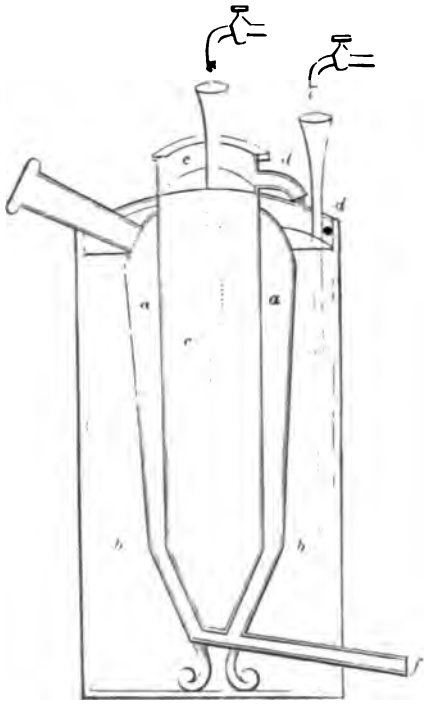
The Beindorf condenser.

necting with a common outlet tube; by unscrewing the upper half of the globular chamber into which the vapor first passes, all the tubes can be thoroughly cleansed. The *Mitscherlich condenser*, Fig. 164, differs from others in keeping the vapor in contact with two separately cooled surfaces, which insures more rapid condensation; as shown in the illustration, the condensing chamber consists of a somewhat tapering cylindrical vessel, *a*, ending in a tube, the whole made of metal (preferably block-tin), and resting on a support in a large metal or wooden case, *b*; into this condenser is accurately fitted at the shoulder a similar metal cylinder, *c*, cone-shaped at the closed end. By means of long funnel tubes cold water is continually supplied at the bottom of the outer and inner coolers, *b* and *c*, which rises as it becomes warmed, and flows out at the top at *d* and *d*; the distillate flows off into a receiver at *f*. In practice, the Mitscherlich condenser has been found very effective, and if the inner cooler has been properly fitted

to the condensing chamber, no escape of vapor need be feared; it is readily taken apart and cleaned, and the only apparent disadvantage lies in the double water supply and waste.

It frequently happens, when distilling from glass flasks or retorts, that the liquid, although boiling at first quietly, suddenly begins to evolve vapor violently, the phenomenon repeating itself from time to time. This outburst of accumulated vapor is termed *bumping*, and although its true cause has not yet been satisfactorily explained, it is known to occur chiefly in smooth glass vessels; it is both annoying and dangerous, as it may result in fracture of the vessel, or in the liquid splashing upward into the condensing tube. Bumping may be due to unequal heating of the vessel, for if the flask or retort be covered with a hood of pasteboard or metal, so that the heat be equally diffused, it occurs but rarely and less violently. Another remedy consists in introducing angular bodies into the liquid, such as pieces of pumice-stone or glass, or a long platinum spiral, which will afford a ready means of escape for the vapor from the bottom of the liquid. Prof. Proctor, of England, has proposed as a very effectual remedy, to pass a slow current of air, hydrogen, or carbon dioxide, through the hot liquid; for small operations this may be done by forcing a stream of air, by means of an India-rubber ball bellows, through a glass tube drawn out to a capillary tube and dipping to the bottom of the liquid, while heat is being applied. Ebullition is said to go on smoothly so long as this is continued, but bumping will commence as soon as the supply of air ceases. Another plan which has been found very satisfactory, especially in the process of distillation, is the suction of air through the retort by means of an aspirator attached to the receiver.

FIG. 164.

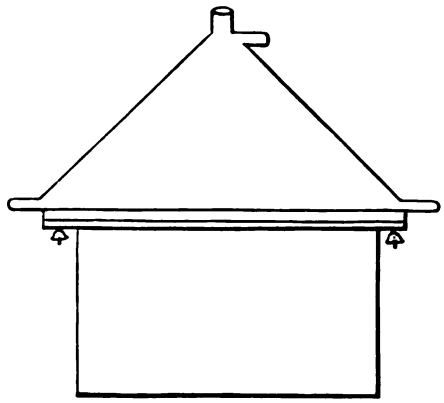


The Mitscherlich condenser

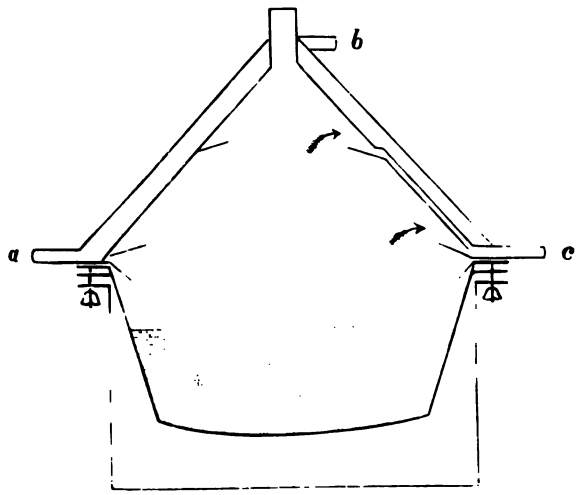
For the recovery of alcohol from weak percolates in the concentration of vegetable solutions by distillation, special metallic stills have been devised. Those made of heavily-tinned copper, of one- to five-gallon capacity, will be found most desirable for pharmacists. Figs. 165, 166, 167, and 168 represent different styles of pharmaceutical

stills in use at the present time. Beck's still (Fig. 165), designed in 1893, is one of the best stills made for the concentration of weak percolates and the recovery of alcohol. It is simple in construction, efficient in condensing power, and easily cleaned. It is made of

FIG. 165.



Beck's pharmaceutical still. (Exterior view.)



(Interior view.)

heavily-tinned copper, and the evaporating pan has a capacity of two gallons. The cold water, which is made to circulate freely between the double walls of the cone-shaped head, is supplied near the base on one side, at *a*, and discharged at the top on the other side, at *b*. The vapor is condensed on the under side of the still-head, the distillate

collecting in two gutters or troughs, one above the other, whence it is discharged through a common outlet, *c*, as shown in Fig. 165. The water-bath and condenser are securely clamped together by means of six bolts and nuts, the rim of the evaporating pan being interposed between two flat rubber rings, and an air-tight joint thus produced. A small tube on the side of the water-bath is for the escape of steam, and if about one and a half gallons of water be put into the bath when the still is started, it will not require refilling for about twenty-four hours. If the quantity of liquid to be distilled is in excess of the capacity of the evaporating dish, the latter may be refilled by means of a long-stem funnel through the opening in the apex of the still-head. The Beck still can be heated with either gas or oil, and if water attachments are not convenient, a barrel of cold water may be placed at some height above the still, from which the condenser can be supplied.

The special features of the Remington still (Fig. 166), are the peculiar shape of the still-head and the construction of the condenser. In the former, the opening for the passage of the vapor is drawn over

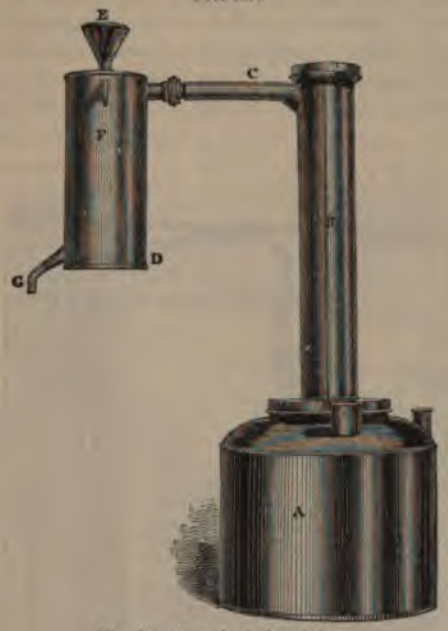
FIG. 166.

The Remington still.

to one side, instead of being in the centre as usual, by which arrangement the condensing surface of the head is greatly reduced and condensation of vapor within the body of the still obviated as far as possible. The condensing tube represents a multiple Liebig condenser, seven block-tin tubes being so arranged within a copper case that cold water is constantly circulating between them. Two ground

brass joints are used—one at the point of juncture of the condenser with the still-head, the other where the nose-piece is attached to the

Fig. 167.



The Prentiss alcohol-reclaimer.

end of the condenser. The capacity of the still is three gallons, and by the siphon arrangement shown in Fig. 166 it is possible to feed the still from a reservoir while distillation is in progress.

Fig. 168.

The Anderson automatic still.

The Prentiss Alcohol-reclaimer (Fig. 167) is easily operated. It is made of tinned copper, and is provided with an upright column, B,

screwed to the top of the still, in which is placed a rod carrying a series of perforated tin disks intended to increase the alcoholic strength of the distillate by condensing the aqueous vapor, which then returns to the still, while the vapor of alcohol passes on to the condenser proper. The vapor passes from the column through a short tube, C, to the condenser, which consists of a twelve-ounce copper can, D, containing a tube bent zigzag, and supplied with cold water by means of a funnel tube, E, reaching to the bottom of the can. The dis-

FIG. 169.

100-gallon copper still, with upright condenser.

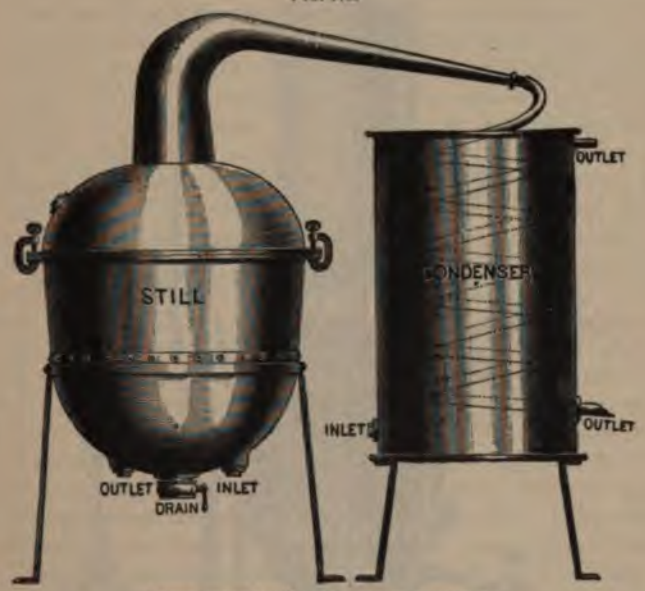
tillate is collected at the outlet, G, a continuation of the zigzag condensing tube, while the waste-water flows out at F, which is connected with the sink by means of rubber tubing.

The Anderson Automatic Still, Fig. 168, differs from the others described, in the continuous automatic supply of water to the water-bath. The refrigeration of vapor is effected by a free circulation of water between the walls of the cone-shaped condenser, as in the Beck still, the distillate collecting in a gutter at the base of the cone. The water in the condenser gradually becomes warm and flows into the water-bath, which is kept filled to a uniform height by means of

an overflow pipe, and thus the necessity of replenishing the boiler with cold water from time to time, in large operations, is obviated. The liquid to be distilled is heated in a broad, shallow evaporating dish, from which the alcoholic vapors rise rapidly, owing to the large extent of surface exposed.

Automatic stills are recommended and largely used for the distillation of water, but, when absolute purity is desired, it must not be overlooked that, in automatic stills, the air and other gases contained in the water are sure to pass out with the steam and redissolve in the condensed vapor, so that, while all non-volatile impurities are

FIG. 170.



Large copper still, with worm condenser.

removed, volatile matter is sure to contaminate the distillate. Distilled water entirely free from air and all other impurities can only be obtained by rejecting the first portion of the distillate (about 10 per cent.), which contains the volatile matter, and allowing the last portion (about 10 per cent.) to remain in the still; this will retain all mineral impurities and such decomposition products as may result from the prolonged action of heat on organic constituents. Only about 80 per cent. of the volume of water to be distilled should be collected and considered absolutely pure. The tubes in which the aqueous vapor is condensed must be of glass or pure block-tin.

In the manufacture of fluid and solid extracts and similar preparations, on a large scale, stills heated by steam are employed for the concentration of weak percolates and the recovery of alcohol from

the dregs. Such stills are made of heavily-tinned copper, and will hold from 50 to 250 gallons of percolate. The boiler, or evaporating pan, is partly enclosed in a copper jacket provided with an inlet and outlet for steam, by which means heat is supplied to the liquid. Figs. 169 and 170 represent two large steam stills of different designs.

Fig. 171.

Still and condenser designed by Dr. Charles Rice.

Condensation of the alcoholic vapor is effected by either a worm or an upright condenser, the latter usually consisting of a number of straight block-tin pipes encased in a copper cylinder, on the principle of the Liebig condenser.

The still designed by Dr. Rice (see Fig. 171) presents the peculiarity of having the condenser situated immediately above the still-head, which is for the double purpose of saving floor-space and allowing the condenser to be used as a reflux condenser in the case of continuous percolation, as explained below. The case enclosing the condensing coil is made of copper, has a rounded bottom, and is closed at the top; cold water is supplied at the bottom at B by means of the rubber tube, A, and is discharged at C, near the top, by means of a tube leading to the waste-pipe, D. The small tube near B, usually closed with a cork, is for the purpose of emptying the water without removing the tube A. The head of the still is provided with three short tubular openings, one for refilling the still when required, another for inserting a thermometer, and the third, shown in the cut, for carrying a safety tube, L. The vapor-pipe starts from the still-head at E, and is connected with the projecting end of the block-tin condensing coil, near the upper part of the tank, at E. The worm inside of the condenser tank has a uniform downward descent, and emerges at F, extending a short distance to the joint, by means of which it is connected with a block-tin pipe, J, leading to the receiving vessel. The head is attached to the body of the still by means of a rubber washer and iron clamps, and can be readily removed, after taking off the clamps, by attaching the tackle, K, to the top of the condenser and hoisting the whole upward. Steam is admitted to the jacket at M, and N is the exhaust pipe for the same. About the middle of the lower projecting end of the condensing tube a branch passes downward back to the still at G, and terminates under the head, in the form of an S, which trap prevents any condensed liquid from flowing back into the still should the stopcock at H be open. The object of this branch pipe is to carry the condensed alcohol back to the still when the apparatus is used for continuous percolation of such substances as nux vomica, aconite, etc. When the still is to be used for this purpose, a large tin-lined copper percolator, into which the moistened drug has been packed and covered with a felt diaphragm, is securely clamped between the head and body of the still, into which menstruum has previously been poured. When steam is admitted to the jacket the alcohol is vaporized, recondensed in the condenser above, and made to flow back to the still and on to the drug in the percolator by means of the branch pipe and stopcock at H, the tube, J, having been disconnected and the joint closed with a cork. The percolate collects in the body of the still and the alcohol is again vaporized as before, the process continuing at the pleasure of the operator, and the drug being thoroughly exhausted with a minimum quantity of menstruum. Thus, prolonged digestion and continuous percolation of large quantities of drugs can be successfully carried on in this apparatus without any loss of alcohol.

The so-called dreg stills for the recovery of alcohol from the marc are sometimes made of 300 or 500 gallons capacity, of heavy copper, but not jacketed; as no injury can be done to the exhausted

material by heat, live steam is passed directly into the still-body containing the marc, and the alcohol is thus rapidly vaporized and forced into suitable condensers.

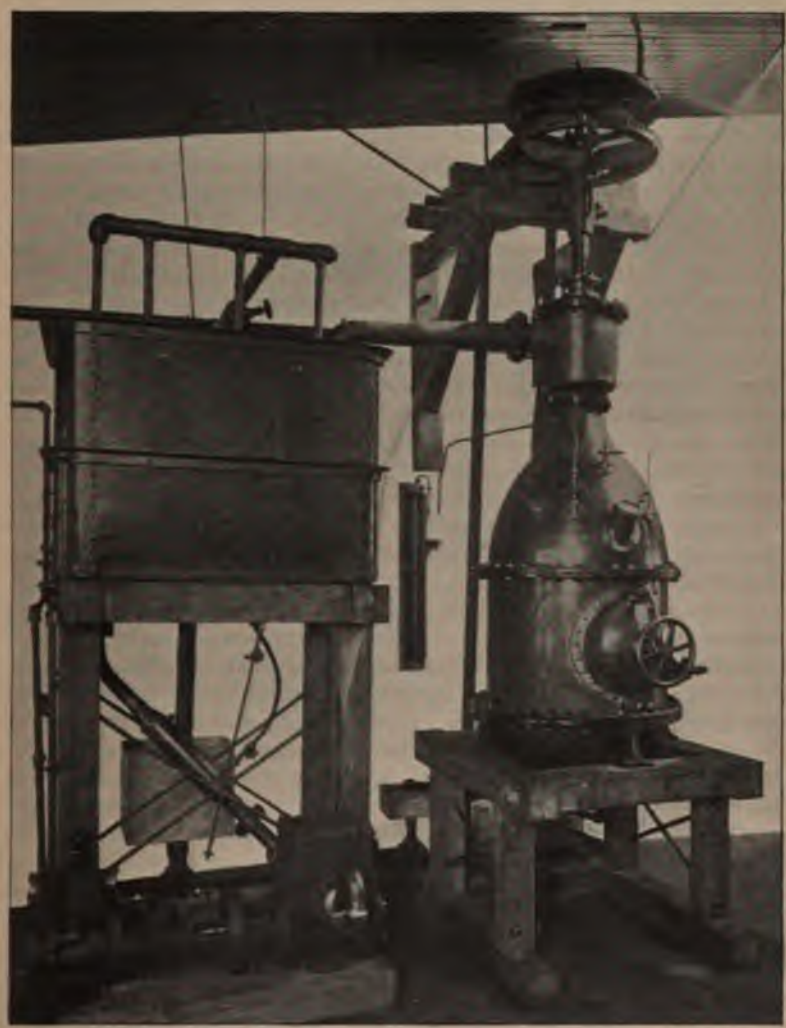
Vacuum stills are necessarily of a somewhat different construction, and, as already stated on page 151, are only used in large manufacturing establishments, where the concentration of bulky vegetable solutions, at low temperatures, is frequently desired. Without the use of vacuum apparatus, the evaporation of solid extracts, without injury, to a condition suitable for powdering, would be an impossibility. Fig. 172 represents a large vacuum still in operation at the establishment of Sharp & Dohme, of this city, to whose courtesy I am indebted for the privilege of giving a photographic reproduction of the apparatus. The still proper consists of an egg-shaped vessel of heavy tinned copper, partly encased in a jacket, to which steam is supplied; it is provided with a vacuum gauge, thermometer, sight-glasses through which the process of evaporation may be watched, and an ingenious stirring apparatus attached to the vertical shaft, operated by means of the two geared wheels seen above the still. The liquid to be evaporated is supplied automatically through the tube seen projecting from the side of the still, to the right of the wheel which operates the clamp holding the man-hole cover in position. Cleaning of the still is effected through a large man-hole in the lower front of the still-body. The vapor of the evaporating liquid passes through the large tube projecting laterally from the still-head, into a series of condensing tubes resting in a large iron tank provided with a constant supply of water; any vapor escaping condensation in these tubes, which may happen on account of its more rapid movement caused by the action of the vacuum pump, will be caught and condensed in the Liebig condenser situated diagonally underneath the iron tank. The distillate is finally discharged through the large spout which may be seen emerging from the valve box connected with the pump about the centre of the lower part of the figure.

The rarefication of air in the apparatus is accomplished by means of an exhaust pump situated under the condensing tank and communicating with the condensing tubes.

When the still is to be operated, the pump is started, exhausting the air from the still until the desired vacuum is reached, as indicated by the barometric gauge attached to the wall between the still and the condensing tank, and connected with the still by means of a two-neck bottle and a block-tin pipe. A rubber hose dipping into the liquid to be evaporated is then connected with the projecting tube to the right of the man-hole, and the stopcock in the tube having been opened, the liquid is allowed to flow into the still by atmospheric pressure until it reaches the desired height in the still, after which the stopcock is partially closed and so set that the supply of liquid is automatically kept up in proportion to its evaporation—the aim being to preserve, as far as possible, the original volume

of the liquid in the still. By this arrangement, large volumes of percolate can be concentrated in a comparatively short time, without taking the still apart or interfering in any way with the distilla-

FIG. 172.



Large vacuum still and condensing tank.

tion of the menstruum. Evaporation taking place at a low temperature and with entire exclusion of air, no possible injury can occur to the constituents in solution.

Fractional distillation is the name applied to a process intended to separate liquids of different boiling-points, and is often a valuable aid in determining the composition of a mixture, or in the purification of certain chemicals. It necessitates the introduction of an accurate thermometer into the retort, flask, or still, so that a change in the boiling-point may be promptly observed and the receiving flask changed accordingly. As all liquids will begin to vaporize before their boiling-point is reached, perfect separation is impossible in a single operation; it is, therefore, customary to collect the liquids condensed during a certain range of temperature in the still, and to subject these again to the same process of fractionation, until finally a pure liquid showing a stationary boiling-point is obtained. As an example, may be cited a mixture of ether, chloroform and alcohol. If pure, the three liquids will boil at 37° C., 60.5° C., and 78° C. respectively; but a mixture may possibly boil at about 40°, when all of the ether will distil over, together with small portions of chloroform and traces of alcohol. As the temperature rises to 65° C., the distillate will consist of chloroform mixed with small portions of alcohol; and finally, at 78° C., alcohol alone will distil over. By changing the receiving flask at 40° C. and 65° C., fractions will be obtained entirely different in composition from the original. If the first fraction be now distilled, the liquid will probably boil near 38° C., and by carefully watching the thermometer and changing the receiver, ether almost entirely free from chloroform and alcohol may be obtained. By thus carefully collecting the fractions at fixed temperatures and re-distilling each by itself, more thorough separation is possible.

During the ebullition of a pure liquid no change of temperature will be indicated by the thermometer, but in a mixture of inter-soluble liquids, a gradual rise will continue as the more volatile are vaporized, this rise being slow or rapid as either the more volatile or less volatile liquids predominate. If a mixture of only partly miscible liquids be subjected to distillation, the temperature will remain stationary during the ebullition of the more volatile liquid and only begin to rise when the same has nearly all been vaporized. In such cases almost perfect separation can be effected, particularly if the boiling-points of the liquids lie far apart. Examples: benzin and alcohol, or alcohol and oil of turpentine. Numerous coal-tar products are obtained by fractional distillation.

Fractional condensation is closely allied to fractional distillation, and is largely employed in the rectification of alcohol and the purification and concentration of glycerin and other liquids. It is effected by passing the mixed vapors into a series of condensers kept at regular temperatures, each succeeding one being cooler than the one which precedes it.

Destructive distillation is the process of heating dry vegetable or animal matter, in suitable closed vessels, until everything volatile has been expelled and a fixed residue is left. As the name indicates, the

process involves the destruction of the original compound, whereby products of simpler composition are obtained. In order to avoid oxidation, destructive distillation must be carried on in closed apparatus with entire exclusion of air, and as the heat necessary is in most cases far greater than that to which glass vessels could be safely exposed, iron retorts or cylinders are employed. The residue left in the iron retort is often a fused mass insoluble in water, which necessitates mechanical means for its removal. The products of destructive distillation, in their crude state, are usually accompanied by a peculiar smoky odor called *empyreuma*, said to be due to an oil developed during the process of decomposition; this is subsequently removed by rectification. The most striking examples of destructive distillation are the manufacture of acetic acid from wood and of illuminating gas from coal.

Sublimation.

Sublimation is the term applied to the process of vaporizing volatile solids and condensing the vapor back into a solid; it must not be confounded with the term *dry distillation*, which is frequently used in place of destructive distillation. The product of sublimation is known as a sublimate, and may occur either in the form of a fine powder or compact masses.

The object of the process of sublimation may be the purification of a substance by separating the volatile solid from less volatile or fixed impurities, as in the case of sulphur, camphor, naphtalene, and iodine, or the separation and collection of volatile solids resulting from chemical reaction at higher temperatures, as in the case of pyrogallol, calomel, and mercuric chloride.

The apparatus consists of a subliming vessel made of iron, glass, or earthenware, and a condenser adapted to the volatility of the product, the condensing surface being kept sufficiently near the source of heat to avoid cooling of the vapor before it reaches the condenser. If the temperature of the condenser is but little below that of the subliming vessel, the vapors of the volatilized substance will not condense until they strike the surface of the condenser, and will form in compact masses, frequently in crystalline condition; as for instance, arsenous acid, corrosive mercuric chloride, ammonium carbonate, and commercial sal-ammoniac. In order to obtain the sublimate in the form of powder, the air in the condenser must be decidedly cooler than the temperature at which the substance volatilizes, because then the vapor will be immediately cooled and rapidly deposited in very small particles, as in the case of calomel, sulphur, and camphor when intended for subsequent compression.

The process of sublimation is confined to the larger operations of the manufacturing chemists, but can be demonstrated in a small way by placing a few grains of camphor or iodine in a long test-tube and then heating until all has been volatilized; in a few minutes the substance may be gathered in the form of very small crystals from the upper part of the tube.

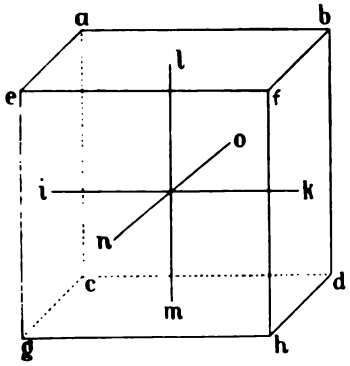
CHAPTER XI.

CRYSTALLIZATION.

THE subject of crystallization, while a most important branch of mineralogy and chemical physics, is of less value in pharmacy proper; but, as the Pharmacopœia makes frequent use of terms belonging to the study of crystallology, and as the pharmacist may have occasion to resort to crystallization for the purpose of determining the character and quality of substances, a short notice is deemed desirable.

Crystallization may be looked upon as another method of separation, as it is frequently employed for the purpose of removing impurities from crystallizable substances. The term *crystal* is applied to solid inanimate bodies of regular internal structure and definite geometrical form, bounded by plane surfaces and having angles of fixed and constant values. The assumption of such distinctive geometrical forms occurs, as a rule, during the change taking place in the state of aggregation of substances from the gaseous or liquid to the solid condition; in a few cases it occurs also in solid bodies, as iron and brass wire.

FIG. 173.



In the preliminary study of crystallography, the meaning of the following terms must be considered.

Faces are the plane surfaces bounding the crystal (see *abdc*, *efhg*, *abfe* and *bfhd*, Fig. 173).

Edges are the lines of intersection of two adjoining faces (see *ef*, *ab*, *fh*, *bf*, *db*, *eg*, *ea*, *gh*, *gf*, *cd*, *ca*, *cg*, etc., Fig. 173).

Angles are the points formed by intersection of three or more faces (see Fig 173), *e*, formed by *abef*, *eacg*, and *efhg*; *f*, formed by *bdhf*, *baef*, and *efgh*; *c*, formed by *dhgc*, *abdc*, and *aegc*, etc.

Axes are imaginary lines drawn through the centre of the crystal, around which the symmetrical deposit of matter has occurred during the formation of the crystal (see *ik*, *lm*, and *no*, Fig. 173).

Amorphous (without form) designates the absence of crystalline form and structure, as in acacia, starch, gelatin, etc.

Di- or *tri-morphous* (of *two* or *three* forms), indicates that the sub-

stance occurs in two or three distinct crystalline forms, as carbon, sulphur, etc.

Polymorphous means of many forms.

Isomorphous (of the same form) indicates that two or more substances to which the term is applied, crystallize in the same form; thus the chlorides, iodides, and bromides of sodium and potassium are isomorphous. Isomorphous bodies are known to resemble each other also in chemical composition, and to permit of a ready interchange of constituents, as in the case of the various alums.

Cleavage is the tendency of most crystals to split in particular directions, affording usually even and frequently polished surfaces, the direction being always parallel with the planes of the axes, or with others diagonal to these. While some crystals cleave very easily, in others this tendency is scarcely discernible.

Tabular crystals are such as crystallize in flat plates, as potassium chlorate, iodine, strontium iodide, etc.

Laminar crystals are such as crystallize in thin plates, as acetanilid, naphtol, calcium hypophosphite, etc.

Acicular crystals are such as occur needle-shaped, as aloin, cinchonidine sulphate, quinine salts, etc.

Prismatic crystals are such as resemble a prism, being extended chiefly in the direction of the longest axis, as salicylic acid, santonin, cinchonine sulphate, etc.

Orthometric refers to the measurement of the angles, and is used to signify that the three axes intersect each other at right angles.

Clinometric refers to the intersection of the axes at oblique angles.

Holohedral, applied to crystalline forms, signifies that the full number of faces required by perfect symmetry are present.

Hemihedral signifies that only one-half the number of faces required by full symmetry are present.

Crystals are formed according to fixed laws of Nature, and there can be no doubt that the force of cohesion plays an important part in their formation; but no one knows how, or why, the molecular particles of certain substances arrange themselves into symmetrical deposits, around a common centre, in a manner to give rise to numerous distinct and definite forms.

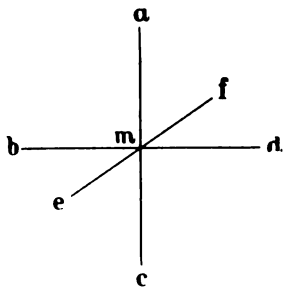
The large variety of forms in which crystals appear, depends entirely upon the number and length of the axes and their relative inclination—that is, the angles at which they intersect each other. All crystalline forms have been reduced by scientists to two main groups, the *orthometric* and the *clinometric* groups (see above), and these have again been subdivided into six systems; the orthometric group comprises the *regular*, *quadratic*, *rhombic* and *hexagonal* systems; the clinometric group, the *monoclinic* and *triclinic* systems. As all crystals belong to one or the other of these systems, the salient features of each should be studied.

1. *The Regular System*, also known as the Monometric, Cubic, Octohedral, or Tessular System.

Crystals of this system have three axes of equal length, which intersect each other at right angles, as shown in Fig. 174.

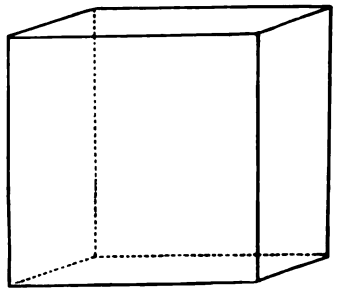
The fundamental forms of this system are the cube and the octohedron, Figs. 175 and 176.

FIG. 174.



Axes of the *regular* system.

FIG. 175.

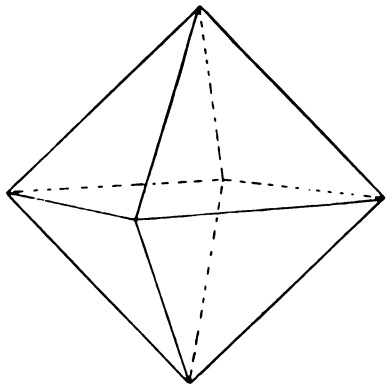


The cube.

Alum, phosphorus, arsenic trioxide, diamonds, alkali iodides, chlorides, fluorides and cyanides, as well as many metals and their sulphides, crystallize in this system.

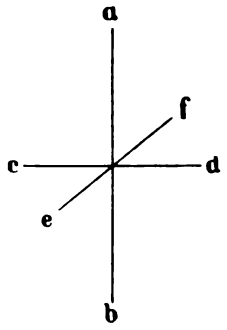
2. *The Quadratic System*, also known as the Dimetric, Square Prismatic, or Tetragonal System.

FIG. 176.



Regular octohedron.

FIG. 177.



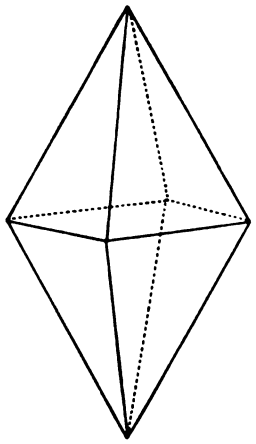
Axes of the *quadratic* system.

Crystals of this system have three axes intersecting each other at right angles, two of which are of equal length, and one either longer or shorter than the other two; the two equal axes are called secondary axes, while the third is termed the primary axis. See Fig. 177.

The fundamental forms of this system are the quadratic octo-

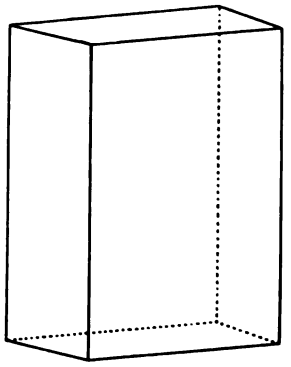
hedron (also called square-based double pyramid) and the right-square prism, Figs. 178 and 179. The pyramids of this system have square bases.

FIG. 178.



Quadratic octohedron.

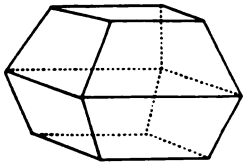
FIG. 179.



Right square or quadratic prism.

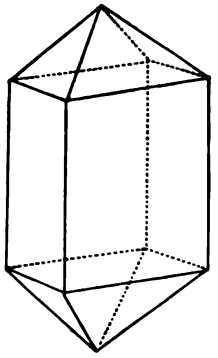
Among the modified forms are the truncated quadratic octohedron, Fig. 180, and the quadratic pyramidal prism, Fig. 181.

FIG. 180.



Truncated quadratic octohedron.

FIG. 181.



Quadratic prism with pyramidal ends.

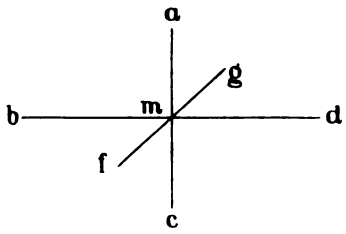
Potassium ferrocyanide, calomel, nickel sulphate, boron, tin, stannic oxide, magnesium sulphate, zinc sulphate, etc., crystallize in this system.

3. *The Rhombic System*, also known as the Trimetric or Right Prismatic System.

Crystals of this system have three unequal axes intersecting each other at right angles, shown in Fig. 182. The fundamental form of this system is the rhombic octohedron or right rhombic double pyramid. See Fig. 183. A modified form is the rhombic six-sided prismatic pyramid, Fig. 184.

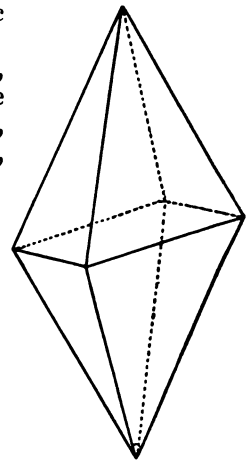
Potassium sulphate and nitrate, resorcin, zinc sulphate, citric acid, iodine, rochelle salt, mercuric chloride, barium chloride, tartar emetic, codeine, salicylic acid,

FIG. 182.



Axes of the *rhombic* system.

FIG. 183.

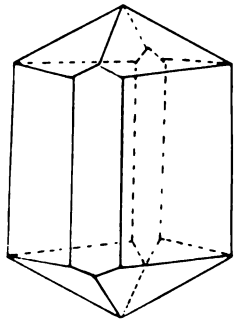


Rhombic octohedron.

piperin, Epsom salt, silver nitrate, ammonium sulphate, cream of tartar, etc., crystallize in this state.

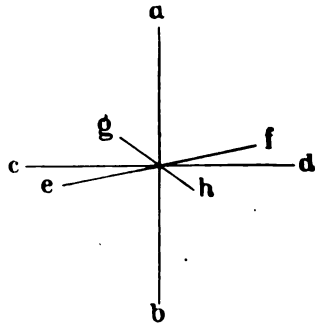
4. *The Hexagonal or Rhombohedral System.* Crystals of this system have four axes, three of which are of equal length and are called secondary axes, whilst the fourth, known as the primary axis,

FIG. 184.



Rhombic prism.

FIG. 185.



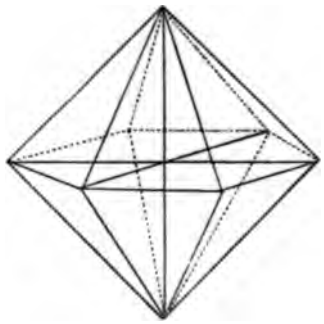
Axes of the *hexagonal* system.

is either longer or shorter than the other three. The primary axis is at right angles to the plane of the secondary axes, which intersect each other at acute angles. See Fig. 185.

The fundamental form is the double six-sided pyramid, Fig. 186.

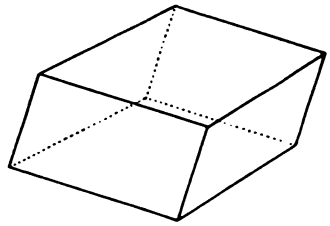
The rhombohedron, Fig. 187, and the regular six-sided prism, Fig. 188, are modifications of this system.

FIG. 186.



Double six-sided pyramid.

FIG. 187.

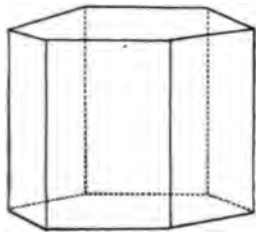


Rhombohedron.

Sodium nitrate, camphor, graphite, ammonium chloride, ice, calc-spar, thymol, metallic bismuth and antimony, arsenic, silicic acid, etc., crystallize in this system.

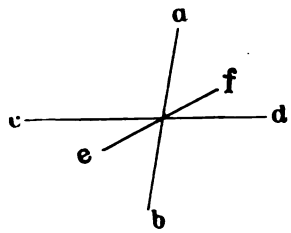
5. *The Monoclinic System*, also known as the Monosymmetric, Clinorhombic or Oblique Prismatic System.

FIG. 188.



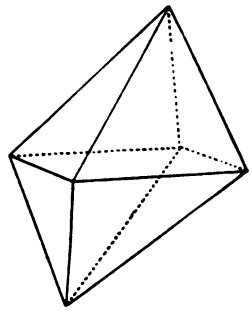
Six-sided prism.

FIG. 189.



Axes of the *monoclinic* system.

FIG. 190.



Monoclinic double pyramid.

Crystals of this system have three unequal axes, two being obliquely inclined to each other, the other axis forming right angles with these two. See Fig. 189.

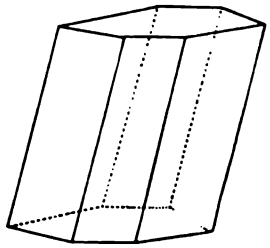
The fundamental forms of this system are the monoclinic double pyramid or octohedron, Fig. 190, and the monoclinic prism, Fig. 191.

Ferrous sulphate, borax, lead acetate, cupric acetate, tartaric acid, potassium chlorate and sodium acetate, sulphate, thiosulphate, phosphate and carbonate, crystallize in this system.

6. *The Triclinic System*, also known as the Asymmetric, Clinorhombohedral, or Doubly Oblique Prismatic System.

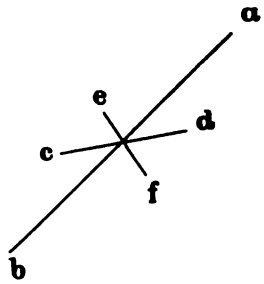
This is the least regular of all the systems, the crystals having unequal axes, all obliquely inclined to one another. See Fig. 192.

FIG. 191.



Monoclinic prism.

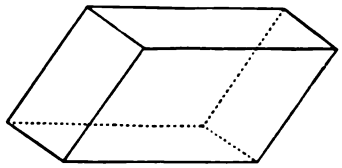
FIG. 192.



Axes of the *triclinic* system.

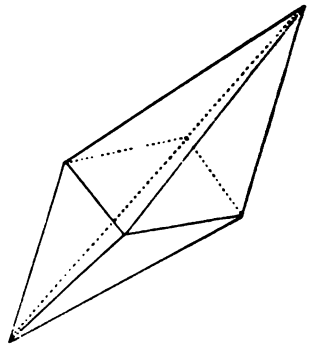
The fundamental forms of this system are the triclinic prism, Fig. 193, and the triclinic octohedron, Fig. 194.

FIG. 193.



Triclinic prism.

FIG. 194.



Triclinic pyramid.

Cupric sulphate, potassium dichromate, gypsum, boric acid, manganous sulphate, etc., cystallize in this system.

The pyramidal form of crystals is found in all the systems above described, while the cube is confined to the regular system, and prisms are met in all but the regular system. The proper classification of a crystal may be determined by measurement of the angles and subsequent calculation of the length and inclination of the axes; the instrument used for this purpose is known as a goniometer.

Various methods are employed for obtaining crystals, dependent upon the nature of the substance to be crystallized: thus, by sublimation; by deposition from supersaturated solutions as they cool; by deposition from solutions during slow evaporation of the solvent; by precipitation; by fusion and partial cooling; by the action of a galvanic current upon a solution; and by the addition of a substance having a strong affinity for the solvent, thereby withdrawing it from the solution. The method generally followed is the gradual separation from supersaturated solutions as they cool; if a solution

of saline matter made with aid of heat is allowed to cool slowly, the water will gradually evaporate, and in some cases a part of it will unite intimately with the soluble substance to form crystals. Water which is thus appropriated, and which is essential to the constitution of the crystals, is called *water of crystallization ;* it varies greatly for different substances, ranging from 5 to 60 per cent. of the weight of the crystals. Crystalline bodies in which this water is entirely absent are said to be anhydrous. Some salts combine with various proportions of water of crystallization according to the temperature at which crystallization takes place, the crystals assuming different forms according to the amount of water taken up; sodium carbonate, sodium phosphate, and zinc sulphate, are examples of this class.

Some crystals will part with a portion of their water of crystallization when exposed to the air, particularly if the latter is slightly warm; they gradually lose their transparency and the surface becomes opaque from a deposit of dry powder. This change is termed *efflorescence*, and is frequently observed in Epsom salt, sodium carbonate, and borax. Other crystals are inclined to absorb moisture from the atmosphere, and in some instances even to such an extent as to liquefy; the terms *hygroscopic* and *deliquescent* are used to designate this peculiar property, the latter applying to the more aggravated form. Potassium hypophosphite, zinc chloride and iodide, potassium acetate and carbonate, and lithium bromide, are examples of deliquescent crystals. As a rule, crystals containing water of crystallization do not absorb moisture from the air, although calcium chloride, potassium citrate, and sodium hypophosphite are marked exceptions.

Besides the water needed for crystallization, some is also at times mechanically retained within the crystal during the formation of the latter, and is violently expelled upon application of heat; such water is called *interstitial water*, because it fills small interstices or spaces in the crystal, and *water of decrepitation*, because it causes the crystals to decrepitate or crackle when heated, due to slight explosions caused by the escape of aqueous vapor from a confined space. It is impossible to crystallize all of the substance held in solution, by a single operation—a portion will remain in solution in some of the water, and this liquid constitutes the *mother-liquor*, which also retains the more soluble impurities. By further concentration the mother-liquor can be made to yield fresh crops of crystals.

The time necessary to complete crystallization will vary with the nature of the dissolved body; the end may be assumed to have been reached when the solution has attained the temperature of the surrounding atmosphere, and the time for this must vary, since the dissolved body, by again taking on the solid form, is continually giving out latent heat to the surrounding solution, and thus the actual cooling is retarded. For small quantities and not very soluble substances, twenty-four to thirty-six hours should be allowed, while large volumes of solution of readily soluble matter will require from three to six or eight days.

In order to obtain large and well-formed crystals the solution should not be made too concentrated, and should be carefully filtered to obtain a perfectly clear liquid, which should be allowed to remain undisturbed and protected against dust, in a moderate temperature; it is the very slow evaporation of the solvent that enables the particles of dissolved matter to arrange themselves harmoniously and symmetrically around the centre of the crystal forming. Perfect rest is equally essential, as agitation of the crystallizing solution tends to disturb the gradual uniform deposit and causes the formation of small and imperfect crystals, as in the case of commercial magnesium sulphate, zinc sulphate, etc.

The proper degree of concentration of the solution must be determined by the solubility of the substance to be crystallized. If the substance is only moderately soluble, the solution may be evaporated until a crystalline crust or pellicle begins to form on the top of the liquid; but in the case of very soluble substances such a degree of concentration would be too great, and a better plan is to evaporate the solution until a small portion transferred to a glass plate crystallizes within a reasonable length of time. In large operations, the manufacturer relies upon the density of the solution as indicated by the hydrometer, and evaporation is continued to such a point as experience has taught to be most desirable for perfect crystallization.

The vessels best adapted for crystallization are deep rough-glazed stoneware basins, called crystallizers, frequently arranged with a lip to facilitate the decantation of the mother-liquor; wooden vats are also extensively employed by manufacturing chemists, and in some cases these are lined with lead. For very small operations, glass or porcelain dishes may be employed, but their smooth surface is not favorable to the deposit of crystals.

Crystallization is often facilitated by placing insoluble foreign substances in the solution, which form starting-points or nuclei for the process, and to which the crystallizing substance readily attaches itself; pieces of string, wire, wood, etc., may be used for the purpose. Sugar is thus crystallized in the form of rock-candy, by stretching strings transversely across the boxes and tubs into which the syrup is poured.

Since crystals do not increase in size from within, as do animals and plants, but grow from without, by deposition of solid matter upon their surface, it is possible to procure large and well-formed crystals, for specimen purposes, by suspending a crystal in a saturated solution of its own constituent matter. This proceeding may be termed *nursing* a crystal. Isomorphous crystals are capable of growing in each other's solution; hence if a crystal of potassium alum be suspended in a solution of ferric alum or chrome alum, the latter will be found uniformly deposited, and thus a complete envelope of chrome or ferric alum will grow on the original crystal of potassium alum.

CHAPTER XII.

CLASSIFICATION OF NATURAL PRODUCTS USED IN PHARMACY.

PLANTS, either spontaneously or after due subjection to various processes, yield certain vegetable substances which are extensively employed in pharmacy, and which, owing to their different behavior as to composition, solubility, etc., have been divided into distinct classes, thus: gums, resins, oleoresins, gum-resins, balsams, fats, essential oils, etc. Unfortunately the names which from long usage have been applied to some drugs are not in all cases indicative of their true nature; hence a knowledge of the characteristics of each class of plant products is essential to guard against errors in nomenclature, which are of daily occurrence in commercial transactions; for instance, the names *balsam of fir* and *balsam copaiba* are applied to substances belonging to the class of oleoresins, and not containing any of the principles which characterize the balsams; *gum guaiac* and *gum mastiche* are pure resins; *gum benzoin* belongs to the class of balsams, and *gum opium* is an inspissated juice of complex composition.

True gums are amorphous exudations wholly soluble in cold water, which are not affected by iodine, but are precipitated by alcohol and solution of lead subacetate, the latter being a most delicate reagent for the presence of gums. Neutral or normal lead acetate is readily miscible with solutions of the true gums, of which acacia may be taken as a type. A class of substances formerly called gums are now more appropriately known as *mucilages*, because they differ in several respects from the true gums; they are not completely soluble in water (cold or hot), but absorb the same, and in some instances swell to a gelatinoid mass. Mucilages are frequently mixed with starch, which is easily detected by the blue color produced upon addition of iodine solution. Tragacanth and the gummy constituents of flaxseed, elm bark, quince seed, etc., belong to the class of mucilages.

Resins are secretory products, in some instances the result of oxidation of volatile oils, and are widely diffused in the vegetable kingdom; they are wholly insoluble in water, except in the presence of caustic alkalies, but are readily soluble in alcohol, ether, and chloroform, and frequently in fixed and volatile oils. Resins are mostly solid and brittle at ordinary temperatures, generally amorphous, readily fusible and inflammable, become negatively electric by friction, decompose before volatilizing, and are precipitated from their solutions by water and acids. Pine resin, mastiche, jalap resin,

and guaiac resin, are examples of this valuable class of plant products.

Oleoresins occupy a position intermediate between resins proper and volatile oils, and partake of the properties of both classes; their existence confirms the view held as to the formation of some resins in plants, and their consistence varies with the relative proportions of resin and volatile oil. Like the resins proper, oleoresins are insoluble in water, but soluble in alcohol and ether; they possess a marked odor, due to the volatile oil present, which latter can be separated by distillation, leaving the resin as a solid residue. White turpentine is an example of solid oleoresins, and copaiba of liquid oleoresins.

Gum-resins exist in plants in the form of an adhesive milky juice composed of variable mixtures of resin and gum suspended in water; they are obtained as exudations, by wounding the stem or root of the plant and allowing the juice to dry spontaneously. The proportion of gum and resin varies considerably, not only for different gum-resins, but also for different samples of the same gum-resin, and those lots are most valuable which contain the largest amount of resin. The activity of the drug resides wholly in the resin, and this fact is taken into consideration in the official formulas for the tinctures of asafetida and myrrh. A peculiarity of all gum-resins is that when properly triturated with water they yield milk-like mixtures termed emulsions, which fact is due to the suspension of very finely divided resin in the solution of gum; these milk-like mixtures cannot be obtained if the commercial finely powdered gum-resins be triturated with water, but require the use of the natural product in coarse powder. As prominent gum-resins may be mentioned asafetida, myrrh, scammony, and ammoniac.

Balsams are either resinous or oleoresinous secretions containing benzoic or cinnamic acid, or both; it is the presence of these acids which distinguishes the balsams from ordinary resins and oleoresins. Balsams are soluble in alcohol, ether, or chloroform, but insoluble in water, although the balsamic principles can be extracted by sublimation or by treatment with hot water. Benzoin and balsam of tolu are examples of resinous balsams, whilst storax and balsam of Peru belong to the oleoresinous variety.

Fats and Fixed Oils.

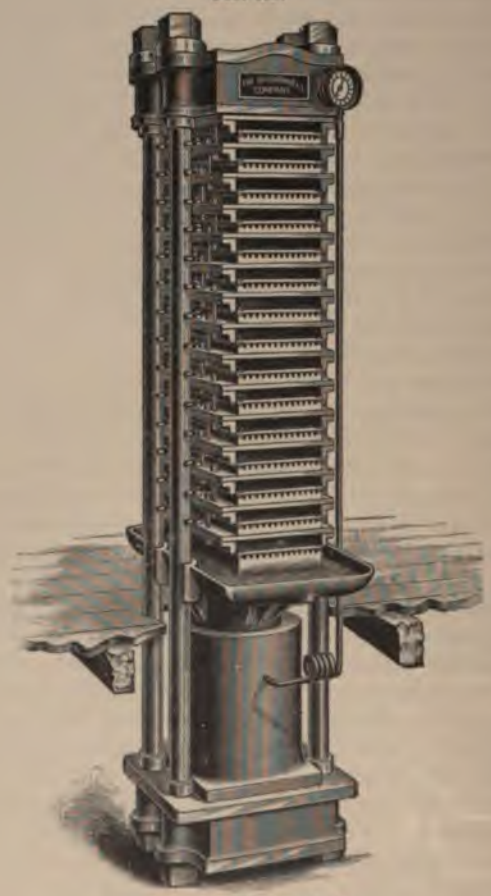
The fats used in pharmacy are derived from the vegetable as well as the animal kingdom, and are divided into fats proper and fatty oils, the latter being known in pharmacy more particularly as fixed oils; when strictly pure they are, as a rule, colorless, odorless, and tasteless. True fats are strictly chemical compounds of glycerin and fatty acids, and are known as olein, palmitin, and stearin, the former being liquid, while the two latter are solid. In fatty oils, olein predominates; while in solid fats, palmitin and stearin are present in greater proportions. Fixed oils, as a rule, are liquid at ordinary

temperature, while fats proper are of a soft consistence and mostly yield liquid fats when subjected to a gradually increased pressure; those of a firmer consistence are usually termed tallows or suets, and such as are brittle at common temperatures are known as waxes, but these are not true fats. The origin of fixed oils in plants is supposed to be the starch, while in animal fats they are more probably derived from albuminous matter. Fats are lighter than water, and insoluble in that liquid; sparingly soluble in cold alcohol, with one or two exceptions; but, as a rule, freely soluble in ether, chloroform, petroleum benzin, carbon disulphide, benzene, etc.; a hot alcoholic solution of fats, in most instances, will deposit them in a crystalline condition upon cooling. All fats, whether liquid or solid, appear greasy to the touch, and when dropped upon paper produce a stain which cannot be dissipated by heat; they have boiling-points varying from 260° to 300° C. (500° to 572° F.), and frequently, when thus heated, undergo decomposition and give off acrid irritating vapors. Fixed oils usually have a specific gravity of from 0.900 to 0.930 at 15° C. (59° F.), though occasionally it runs as high as 0.970, as in the case of castor oil; many oils do not congeal until the temperature has fallen considerably below 0° C. (32° F.), while others deposit solid matter at 10° C. (50° F.). Like water, fixed oils expand upon congealing, and have been known to burst the vessels containing them. Fats are not inflammable, but will burn more or less readily by the aid of a wick. Nearly all vegetable and animal fats consist of a mixture of two or more fats, and when exposed to the air become oxidized, many of them gradually assuming a disagreeable odor, due to the liberation of odorous fatty acids; this condition is known as *rancidity*, and may be avoided by keeping the fats as free from moisture as possible, in air-tight containers stored in a dry, cool, and dark place. Rancid fats may be improved and, to a certain extent, restored, by washing them with warm water, or by treating them with magnesia or other weak alkali, and afterward washing them well. During the oxidation of fats by exposure to air, heat is always developed, and certain fabrics, such as woollen and cotton rags, which are known to be poor conductors of heat, are liable to spontaneous ignition if saturated with fats and exposed to the air for some time. Fixed oils may be conveniently divided into *drying* and *non-drying* oils; the former upon exposure to air gradually thicken, and if in thin layers, form varnish-like masses, whereas the non-drying oils remain fluid and become rancid.

Although fats are found in various parts of plants, those intended for use are collected exclusively from the fruit and seed, and are obtained either by expression or by extraction with some suitable solvent; the former process yields somewhat lower results, but is preferred because less troublesome and productive in many cases of a superior article. In Fig. 195 is shown an hydraulic press extensively used for the expression of mustard, cotton seed, and linseed oils. The crushed material, after being heated somewhat, is placed in sacks

or press-cloths between the series of plates, and pressure applied from below, the oil being collected in the large box or trough, and from there delivered into the receiving vessel. The residue from certain seed expressions is used, under the name of *oil-cake*, as food for cattle and hogs or for fertilizing purposes. Cold expression

FIG. 195.



Steam press for fixed oils.

yields a finer oil than when heat is employed, although slight warming is generally resorted to so as to render the oil more fluid in the seed and thus insure a better flow. Expressed oils are always more or less contaminated with impurities, such as mucilaginous and albuminous matter, which are removed by allowing the oil to settle in large tanks and drawing off the clear liquid. Frequently filtration is employed for improving the quality of the oil, felt or flannel bags

being best adapted for this purpose. When purification of fixed oils becomes necessary they are treated either with sulphuric acid, caustic alkalies, zinc chloride, tannin, or alkali carbonates, and subsequently washed with hot water, after which they are carefully decanted.

The extraction of fixed oils is conducted in specially constructed extractors, frequently so arranged that the solvent is made to act upon successive portions of crushed seed, the saturated solution of fat being then transferred to a suitable distillatory apparatus, where the solvent is recovered, to be again used for subsequent operations. The solvents usually employed are petroleum benzin of low boiling-point and carbon disulphide; the oil is obtained in larger quantity than by expression, and is free from many impurities often found in expressed oils.

Fixed oils are frequently subjected to a bleaching process, which consists in treating the oil with solution of hydrogen dioxide, potassium permanganate, potassium dichromate, chlorine, or sulphurous acid; of these methods, the hydrogen dioxide process is preferable, as it is least liable to injure the oil, while the use of other bleaching agents necessitates repeated washing of the oil with water and even weak alkali solutions to remove acid oxidation products.

The adulteration of fixed oils is effected by mixing the finer and more valuable oils with inferior and cheaper varieties, and as the crude methods of former years are no longer practised, a better knowledge of the chemical behavior of fats and fixed oils is necessary at the present day. Caustic and carbonated alkalies are practically without effect upon fats and fixed oils in the cold unless free acids, due to rancidity, be present; a more or less uniform mixture results, but no chemical change is produced. If boiled together with solutions of alkali hydroxide or carbonate, all fats and fixed oils used in pharmacy, with the exception of lanolin, wax, and spermaceti, readily undergo saponification and form water-soluble compounds; the amount of caustic soda or potassa necessary to saponify *one gramme* of fat varies for each fat and fixed oil, and expressed in *milligrammes* is known as Koettstorfer's saponification factor, by means of which the purity of fixed oils may be tested. Since fatty compounds are capable of uniting with iodine, a method for the detection of admixtures in fixed oils has been proposed by Huebl, the quantity of iodine combining with a given weight of the oil being different in each case; the number of grammes of iodine absorbed by 100 grammes of any fixed oil expresses the iodine addition factor of that oil. (These two methods are more fully explained under the head of Pharmaceutical Chemistry.)

Drying oils may be distinguished from non-drying oils by their behavior with sulphuric and nitrous acids. If 50 Gm. of a fixed oil be mixed with 10 Cc. of concentrated sulphuric acid, heat will be developed varying in intensity for different oils, the drying oils always showing the greatest rise in temperature; thus, while olive oil increases 42° C. in temperature, castor oil 47° C., and oil of

almond 52° C., hempseed oil will show a rise of 98° C. and linseed oil 103° C. When mixed with nitrous acid, non-drying oils will gradually be converted into a solid mass, while drying oils remain fluid even after prolonged contact, although a few become somewhat thicker. The test is made by agitating for a short time one part of copper foil with five parts each of nitric acid and the oil, and setting the mixture aside for about six hours, when solidification is generally completed. Among the prominent non-drying oils are olive oil, castor oil, almond oil, lard oil, sesame or benne oil, mustard oil, colza or rapeseed oil, and groundnut oil, while the following belong to the drying oils: linseed oil, cottonseed oil, poppyseed oil, hempseed oil, and walnut oil.

Animal fats are usually obtained by rendering over a slow fire and then straining to remove the particles of membranous tissue; like vegetable fats, they should be preserved in well-closed vessels impervious to fat, in a cool place, protected against moisture and light. Of the fats and fixed oils recognized in the Pharmacopœia, seven are of animal and eight of vegetable origin.

The Official Fats and Fixed Oils.

Adeps. Lard. This is the prepared abdominal fat of the hog derived from the so-called *leaves*, and is preferably collected in the winter or early spring, as it has a higher fusing-point than that collected in summer. It is obtained by removing, as far as possible, all foreign matter, washing well with water after the fat has been cut into small pieces and then melting with a moderate heat, or a steam or water bath, until all water is dissipated. Lard is slightly soluble in alcohol and readily so in ether, chloroform, carbon disulphide, or benzin; it fuses at 38°–40° C. (100.4°–104° F.) to a clear colorless liquid, and at 30° C. (86° F.) again returns to a soft solid. In order to render lard inodorous, to each pound of it melted, fifteen grains of powdered alum and thirty grains of table salt are added, and the heat continued as long as a scum rises; this is removed, the lard is allowed to cool, and then well washed with a constant stream of water until all traces of the salts have been removed. Finally, the fat is remelted and the heat continued until all the water has been evaporated. Lard consists of a liquid fat known as *olein* and a solid fat known as *stearin*, which can be readily separated by expression at low temperatures; the liquid fat is officially employed under the name of lard oil, but the stearin alone is not used in pharmacy. Owing to the presence of these two fats, melted lard when allowed to cool slowly will become granular, the more solid fats partially separating, hence no smooth product can be obtained; lard and its preparations when melted should always be stirred until cool, or at least until a uniform creamy mixture results. Commercial lard is liable to contain starch, alkalies, added to improve the whiteness, and table salt mixed with it as a preservative; these substances the Pharma-

copœia requires to be absent in the medicinal lard, as shown by appropriate tests. Since lard may be adulterated with cottonseed oil, the official silver nitrate test for this admixture should not be omitted. Pure lard is liable to become rancid if kept for some time, hence the Pharmacopœia directs its preservation by benzoinating. This is done by suspending two parts of coarsely powdered benzoin, contained in loosely textured cloth, for two hours, in 100 parts of melted lard at a temperature not exceeding 60° C. (140° F.), in a covered vessel, then straining and cooling. The balsamic principles of benzoin are soluble in the melted fat, and protect it afterward against change. In summer, the preparation which is officially known as Adeps Benzoinatus should contain 5 per cent. of white wax, in place of a like quantity of lard, to render it firmer.

Adeps Lanæ Hydrosus. Hydrous Wool-fat. Lanolin. The official article is a mixture of 70 per cent. of purified wool-fat and 30 per cent. of water. The wool of sheep contains a natural grease, which is readily removed in the process of washing the wool, and is of complex composition, containing about 30 per cent. of free fatty acids, besides numerous fatty compounds; the so-called cholesterin fats are the constituents sought for the production of lanolin. The crude fat is first treated with weak alkaline solutions, whereby a creamy mixture is obtained, which is placed in centrifugal machines and separated into two layers; of these the upper layer is treated with calcium chloride, which precipitates impure lanolin, to be purified by repeated melting and washing. Final extraction with acetone yields pure anhydrous lanolin of yellowish brown color and characteristic odor, which, when mixed with 30 per cent. of water, constitutes the official hydrous wool-fat. The chief advantage of lanolin over other fats lies in its miscibility with large amounts of water (twice its weight) without losing its ointment-like character. The Pharmacopœia demands for the official article the entire absence of alkalies, glycerin, and free fatty acids. Hydrous wool-fat has about the same fusing-point as lard, and forms turbid solutions with ether and chloroform; it is saponified with difficulty.

Cera Alba; Cera Flava. White Wax; Yellow Wax. Beeswax. The only wax recognized by the Pharmacopœia is that secreted by the bees and used by them in the construction of the honeycomb. To obtain the wax, the honey is drained from the comb, which is then expressed, melted in water, and after the impurities have subsided, run into moulds and cooled. This constitutes yellow wax, from which white wax is made by a process of sun-bleaching, as follows: Melted wax is again solidified in the form of thin ribbons or bands, by allowing it to flow over wet revolving cylinders; these bands are moistened with water, and exposed to sunlight in the open air. After exposure for some time the color disappears in spots and the wax is again melted, re-solidified and treated as before, the process being repeated from time to time until the wax is completely bleached, when it is finally melted and run into moulds; besides losing its color,

wax thus treated is somewhat changed by long exposure to light and air, and is more disposed to rancidity than yellow wax, as is noticeable in the modified odor. Pure yellow wax melts at 63°–64° C. (145°–147.2° F.), white wax at 65° C. (149° F.); they differ from true fats in not containing glycerin, and in not forming soap when boiled with solution of alkali carbonates. Wax is completely dissolved by ether and chloroform, but not by boiling alcohol and cold benzene or carbon disulphide. Besides the crude adulterations readily observed in melted wax, tallow and other fats, as well as vegetable wax, resin, and paraffin, are frequently mixed with it; they can be quickly detected by the pharmacopœial tests. Fats and resin may be taken up by a boiling solution of sodium hydroxide or by petroleum benzin, neither of which dissolves the wax; paraffin is readily detected by heating the suspected wax with concentrated sulphuric acid, which destroys the wax but leaves the paraffin unaffected. If pure wax be melted and allowed to cool slowly, it will always congeal with a level surface, but if paraffin in any form be present, the surface will be more or less concave, according to the extent of adulteration.

Cetaceum. Spermaceti. Spermaceti is obtained by expression from the fatty secretion found in the cranial cavity of the sperm whale. Before the animal is killed, the fat is liquid, but afterward congeals to a yellow mass; by expression a yellow oil is removed, the residue is melted, washed with weak potassa solution and water, and finally allowed to congeal. Spermaceti is apt to become yellowish and rancid by age and when exposed to air; it melts at about 50° C. (122° F.), and is soluble in boiling alcohol, ether, chloroform, carbon-disulphide, and fixed and volatile oils. It can be powdered by trituration in a mortar after sprinkling with alcohol. Fused with potassa, spermaceti is saponified, but not if boiled with a solution of alkali carbonate, which fact serves to detect the presence of stearic acid as an adulteration.

Oleum Adipis; Lard Oil. The fixed oil expressed from lard at a low temperature. It congeals near 0° C. (32° F.), but already at 10° C. (50° F.) begins to deposit granular fat, hence, to remain fluid, it should be kept at or above 15.5° C. (60° F.) The most likely adulterations are cottonseed oil and paraffin oils; the former can be detected by heating the oil with an acidulated alcoholic solution of silver nitrate, when the mixture should remain colorless. Lard oil should be perfectly saponified by heating with potassa, water, and alcohol; the separation of an oily layer would indicate paraffin oils. The yield of lard oil is equal to about 60 per cent. of the weight of the lard expressed.

Oleum Amygdalæ Expressum. Expressed Oil of Almond. This oil, also commercially known as oil of sweet almond, is obtained by expression from the bitter as well as the sweet almond, the yield from the latter source being about 20 per cent. greater than from the former. The yellowish color of the commercial oil is due entirely

to the colored episperm, for if blanched almonds be expressed, a colorless oil will be obtained. Expressed oil of almond is soluble to some extent in cold alcohol; it remains perfectly clear at —10° C. (14° F.), and does not congeal until cooled to —20° C. (—4° F.). The oil is largely adulterated with the oils of peach and apricot kernels, which can be detected by shaking together 1 volume each of fuming nitric acid and water and 2 volumes of the suspected oil; a whitish mixture, free from orange or reddish color, results if the oil is pure. The development of a brownish color, with the same test, would indicate the presence of cottonseed, groundnut, sesamum, or poppyseed oils.

Oleum Gossypii Seminis. Cottonseed Oil. The official cottonseed oil is a refined bleached oil, for the crude product, obtained by hydraulic pressure from the seed, has a brown color and linseed-like odor, and contains considerable quantities of albuminous matter. After subsiding, the crude oil is treated with superheated steam, and finally well shaken with heated weak alkali solution. The yield of oil from cottonseed varies from 12.5 to 20 per cent.; the residue, or oil-cake, is considered a valuable cattle food and fertilizer. Cottonseed oil congeals when cooled to 0° or —5° C. (32° or —23° F.), and is instantly colored dark reddish-brown in contact with concentrated sulphuric acid; it belongs to the drying oils, but shaken with nitric acid and water it gradually forms a colored semi-solid mass. The chief use of cottonseed oil is as a substitute for more expensive fixed oils, as in the case of some of the official liniments, and there is no doubt that it is extensively employed as an adulteration for almond, olive, and other oils. When heated with an acidulated alcoholic solution of silver nitrate the oil assumes a reddish-brown color, which serves as a test for its detection.

Oleum Lini. Linseed Oil. The Pharmacopœia demands an oil expressed without heat, which, as a rule, is not readily obtainable, since hot pressure increases the yield nearly 50 per cent. Extraction with petroleum benzin or carbon disulphide shows still better results: thus, cold pressure, 16 to 20 per cent.; hot pressure, 22 to 28 per cent.; extraction, 33 per cent. Cold-pressed linseed oil is lighter in color than the other varieties; when boiled it darkens in color and thickens, losing about 6 to 8 per cent. in weight. The oil is quite soluble in absolute alcohol, and forms a clear mixture with an equal volume of official alcohol, but becomes turbid if the proportion of alcohol is doubled; it does not congeal above —20° C. (—4° F.). Linseed oil is always slightly acid and is readily saponified by alkalies; it is the best drying oil known and should not be even partially solidified if shaken with nitric acid and water for a long time, by which means the presence of non-drying oil may be detected. As linseed oil may be adulterated with paraffin oils, the Pharmacopœia recommends shaking an aqueous solution of linseed oil soap with an equal volume of ether, which latter, after decantation, should not show a bluish fluorescence nor leave an oily residue upon evaporation.

Oleum Morrhuæ. Oleum Jecoris Aselli. Cod-liver Oil. Medicinal cod-liver oil should always be procured from fresh livers, by the aid of a gradually increased steam heat not exceeding 60° C. (140° F.); the oil is allowed to separate from the watery fluid, and after it has been frozen is expressed in canvas bags, whereby a pure only slightly colored oil is obtained, the hard yellow residue, consisting of stearin and tissue, being rejected for other purposes. Cod-liver oil thus carefully prepared keeps well in completely filled vessels, and when cooled to 0° C. (32° F.) should deposit no solid fats; it belongs to the drying oils, and if exposed to the air soon thickens and assumes a disagreeable strong odor and taste. The color reactions with sulphuric acid mentioned in the Pharmacopœia are due to the presence of certain biliary constituents and are very pronounced. Cod-liver oil has a slight acid reaction which increases with age. The more probable adulteration consists of seal oil and other fish oils, which can be detected by testing with fuming nitric acid; cod-liver oil turns red, then bright rose-red, and finally lemon-yellow; seal oil shows at first no change of color, and other fish oils become blue at first and afterward brown and yellow.

Oleum Olivæ. Olive Oil. The finest quality of olive oil is that obtained by cold expression from the flesh only of the ripe fruit, and is known commercially as "virgin oil;" a second quality is expressed from the residue, after the same has been mixed with water. Good olive oil is of a pale yellow or light greenish-yellow color, while the inferior grades, often expressed from fermented olives, are of a deeper green. It becomes cloudy at 10° C. (50° F.), and congeals at 0° C. (32° F.), to a whitish granular mass. Olive oil is, no doubt, largely adulterated with cottonseed oil, groundnut oil, poppyseed oil, and sesamum oil; when heated with an acidulated alcoholic solution of silver nitrate, the oil, if pure, should retain its original pale-yellow color without becoming reddish or brown. Sesame oil is best detected by a special test given in the Pharmacopœia, and which is characteristic for that oil. A solution of soap made from the suspected oil and potassa is decomposed with sulphuric acid, and the liberated fatty acid, freed from water, is shaken with hydrochloric acid; if the mixture turns green, sesame oil is present, and on the subsequent addition of sugar, the mixture, after shaking, assumes a violet or crimson tint. This is known as Baudouin's test.

Oleum Ricini. Castor Oil. This well-known oil is produced in very large quantities in this country in the city of St. Louis; in order to increase the yield of the oil, the seed is frequently heated to about 60° C. (140° F.), before expression, and the oil afterward heated with water to remove albuminous matter. The yield of oil by cold expression is about 25 to 30 per cent., and by hot expression, 38 to 45 per cent. Castor oil when cooled to 0° C. (32° F.), becomes turbid, but does not congeal until the temperature has been reduced to —18° C. (—0.4° F.); it is soluble in all proportions in absolute alcohol or in glacial acetic acid, and in three times its volume

of a mixture of 19 volumes of alcohol and 1 volume of water, which distinguishes castor oil from other fixed oils. Castor oil is rarely adulterated and is readily saponified by alkalies.

Oleum Sesami. Sesame Oil. Benne Oil. Teel Oil. Sesame oil is obtained both by cold and hot expression to the extent of about 50 per cent. of the weight of the seed. It congeals at —5° C. (23° F.), to a yellowish-white mass, and is converted into a brownish-red jelly when mixed with concentrated sulphuric acid. When shaken with an equal volume of concentrated hydrochloric acid, it assumes an emerald-green color, which, upon addition of sugar and further shaking, changes to blue, violet, and finally, deep crimson. Sesame oil is sometimes found as an admixture in olive oil and expressed oil of almond.

Oleum Theobromatis. Oil of Theobroma. Butter of Cocoa. Oil of theobroma is the only fixed oil recognized by the Pharmacopœia which is solid at ordinary temperature; it is brittle at 15° C. (59° F.), and melts at from 30° to 33°C. (86° to 91.4° F.). The oil is obtained to the extent of about 40 per cent., by heating the shelled seeds to 70° C. (158° F.), and expressing between hot iron plates. Adulterations with stearin, tallow, wax, and paraffin, can be quickly detected on account of the low fusing-point and high congealing-point of the pure oil. The Pharmacopœia requires that 1 Gm. of oil of theobroma dissolved in 3 Cc. of ether at 17° C. (63° F.), and plunged into water at 0.° C. (32° F.), shall neither become turbid nor deposit a granular mass *in less than three minutes;* if the mixture, after congealing, be warmed to 15° C. (59° F.), it should gradually form a perfectly clear liquid.

Oleum Tiglii. Croton Oil. Croton oil is obtained by expression, and does not congeal until cooled to —16° C. (3.2° F.). Its solubility in alcohol increases with age, and it has been shown by Senier, of England, that the portion insoluble in alcohol contains the purgative principle, while the vesicating principle is soluble in alcohol. Croton oil is a non-drying oil, but differs from other non-drying oils, in remaining liquid if vigorously shaken with fuming nitric acid and water and allowed to stand for one or two days; this behavior serves to detect adulterations.

Glycerin.

The sources of all glycerin used in pharmacy or sold commercially, are various fats, both of vegetable and animal origin, glycerin being an invariable constituent of all official fats except spermaceti and beeswax, from which it is liberated whenever such fats are converted into soap by the action of moist metallic oxides. It has proven a most valuable solvent and antiseptic in pharmacy, second only to alcohol in this respect. Nearly all glycerin now produced in this country is made by decomposing fats in large copper digesters; fat and water having been put into the digester, steam under 120 to 150 pounds pressure is introduced for several hours, whereby the mixture is kept in constant

agitation and the fat is completely decomposed, the glycerin entering into solution in the water, and the non-volatile fatty acids floating on the surface of the aqueous solution. The volatile fatty acids are allowed to escape with steam through a small orifice in the top of the digester. The dilute solution of glycerin is transferred to evaporating tanks and concentrated until it reaches a density of 28° Baumé, equal to a specific gravity of 1.24 at 15° C. (59° F.). The crude dark amber-colored glycerin thus obtained is introduced into specially constructed stills, into which superheated steam enters at a temperature of about 250° C. (482° F.), carrying the glycerin, in the form of vapor, with steam, over into a series of condensers so arranged that the glycerin condenses in passing through, at various degrees of density; the first condenser, being least cooled, contains the heaviest glycerin, the distillate becoming gradually weaker, until, in the last condenser, almost pure water is collected. Coloring matter is removed by treatment with animal or vegetable charcoal, and the distillation is frequently repeated two or three times until the required degree of purity has been obtained. The Pharmacopœia demands at least 95 per cent. of absolute glycerin, which liquid has the specific gravity 1.25 at 15° C. (59° F.), and is soluble in water and alcohol in all proportions, as also in a mixture of three parts of alcohol and one part of ether, but is insoluble in ether, chloroform, benzene, petroleum benzin, fixed and volatile oils. The most important tests of those mentioned in the Pharmacopœia are: the absence of turbidity and color, when glycerin, after dilution with water, is heated and mixed with silver nitrate solution, and then exposed to diffused daylight for five minutes; the absence of an offensive or acidulous odor when glycerin is heated with diluted sulphuric acid; the absence of dark color when a mixture of equal volumes of glycerin and concentrated sulphuric acid is *gently warmed*; and the complete volatility of glycerin upon ignition.

Although official glycerin boils at about 165° C. (329° F.), it is readily vaporized from an aqueous solution at 100° C. (212° F.).

Volatile Oils.

Volatile oils are those peculiar principles to which, in a majority of cases, the odor of plants is due; they do not all pre-exist in the plant, some being the result of fermentative action between certain constituents of the plant in the presence of water, and others being produced by destructive distillation. Volatile oils may exist in every part of the plant from the root to the seed, and when several oils are present in different parts of the same plant, they will generally be found to differ in physical as well as chemical properties; as, for instance, the oils of orange obtained from the leaf, flower, and rind. They usually occur in separate cells, as glands in the herbaceous portion and rinds of many fruits, or distributed throughout the interior tissue, or forming distinct oil tubes, as in the fruit of

fennel, anise, etc. The odor of volatile oils, while in some instances due to their particular composition, in others appears to be due to atmospheric influences, since oil of turpentine and others when rectified in an atmosphere of carbon dioxide have been found devoid of all unpleasant odor, and yet, when again exposed to the air, they soon resumed their characteristic odor. With few exceptions, volatile oils are lighter than water, and their solubility in water is very variable; their specific gravities at 15° C. (59° F.), range from 0.850 to 1.185. Absolutely pure volatile oils are colorless, but the commercial varieties are frequently colored yellow, green, blue, red, and brown; the color in most instances disappears when the oil is brought into solution. Many volatile oils are completely soluble in glacial acetic acid, and all are soluble in alcohol, but in proportions varying from less than an equal volume to ten or more. They have but, few properties in common with fixed oils, but like these are soluble in ether, chloroform, and carbon disulphide. Freshly-prepared volatile oils are generally freely soluble in petroleum benzin, but, after exposure, they gradually lose this property and often form turbid mixtures when shaken with the same. When dropped upon filtering paper they cause a stain somewhat resembling that of fixed oils, but which is dissipated upon the application of heat; the stain produced by old or partly resinified volatile oils, frequently cannot be driven away by heat, but can be readily distinguished from the stain of fixed oils, by its shining varnish-like appearance and by its complete removal with the aid of warm alcohol, the stain from fixed oils being devoid of lustre and insoluble in alcohol. Volatile oils are inflammable, and burn with a bright but sooty flame; exposed to air and light they are more or less rapidly oxidized, being gradually converted into a viscid oil and finally even into a solid resin. They never become rancid in the sense mentioned under fixed oils, and do not contain glycerin. Owing to the changes which volatile oils undergo through exposure to light and air, they should be preserved in well-stoppered bottles, in a dark place; amber or yellow-colored glass is best adapted for oil containers, as it intercepts the actinic rays of light. The addition of deodorized alcohol or Cologne spirit will also preserve the fine aroma of such oils as lemon and orange, not more than 5 per cent. by volume being necessary. Resinified oils may be restored by redistillation with water or weak alkali, or, if in small quantities, by Cuvier's method, which consists in shaking the oil for fifteen or twenty minutes with a magma formed of animal charcoal and a solution of borax, whereby the resinified portion is united to the borax and the oil becomes limpid. The whitening of corks in bottles containing volatile oils, is due to the presence of ozone produced by the gradual oxidation of the oil.

The adulterations to which volatile oils are subjected are fixed oils, alcohol, and highly rectified petroleum; frequently, also, the higher-priced oils are mixed with cheaper and inferior oils. Fixed oils are easily detected by a permanent greasy stain upon paper, and

by a non-volatile residue when the suspected oil is subjected to distillation. Alcohol may be tested for in several ways. If the oil be shaken in a graduated tube with an equal volume of water or glycerin, and then allowed to stand at rest, any diminution in the volume of the oil would indicate alcohol, and approximately also the proportion present; if considerable alcohol be present, the characteristic lambent blue flame of burning alcohol will be observed if a portion of the suspected oil is ignited in a dark room; fused calcium chloride and dry potassium acetate are insoluble in volatile oils, but in the presence of alcohol become soft and even liquid, depending upon the proportion of alcohol; potassium acetate and sulphuric acid added to volatile oils will generate acetic ether if alcohol be present, which may be detected by its odor; and aniline-red is insoluble in pure volatile oils, but colors these red in the presence of alcohol. Adulterations with rectified petroleum are often not easily detected, and may require a careful chemical examination; for it, as well as for the inferior volatile oils, the Pharmacopœia prescribes appropriate tests under the head of the respective oils likely to be thus contaminated. The different optical behavior of volatile oils is also often of great value in the search for adulterations.

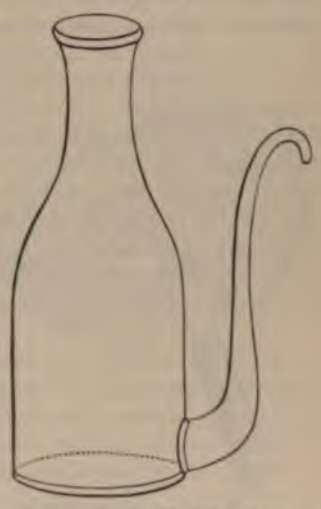
The usual method of obtaining volatile oils is by distillation, and in some instances the plan is still followed of placing the oil-yielding

FIG. 196.

Distillation of volatile oils by steam.

material in an iron or copper still provided with a perforated diaphragm or false bottom, and adding sufficient water to barely cover the material, after which direct heat is applied until the water boils, and then continued as long as the distillate shows the presence of any volatile oil. Although the boiling-points of volatile oils are considerably above that of water, the oils pass over rapidly with the vapor of boiling water, and in the leading establishments in this country and Europe, volatile oils are now distilled by passing steam under pressure into stills which contain the material on a series of perforated trays extending across the inner body of the still; by this method compaction is avoided, the steam can readily penetrate every particle of the material, and a much finer quality of oil results, since prolonged contact with boiling water has a deleterious effect upon many oils. Fig. 196 represents the distillation of volatile oils by steam, as carried on at the factory of Fritzsche Bros., at Garfield, N. J.; the large still in the rear has a capacity of 1000 pounds of cloves. Whenever the volatile oil is deeply imbedded in the material, as in the case of cloves, cubebs, and many barks and seeds, it is necessary that this be first reduced to a coarse powder so as to facilitate the liberation of the oil. The distillate, which is a mixture of oil and water, is collected in suitable receivers, either in the form of Florentine flasks with a single outlet tube near the bottom and reaching nearly to the top, as shown in Fig. 197, or of tall cylinders provided with two tubes, a long one near the bottom and a short one near the top; as the distillate cools it separates into two distinct layers, one consisting of pure oil and the other of water still holding some oil in solution and suspension, which is subsequently regained, either by conveying the water back direct to the still or by distilling the water in separate stills, frequently after addition of table salt to facilitate the separation of the oil. As a rule, the layer of oil floats on top, except in those cases in which the oil has a specific gravity above 1.000, as the oils of cloves, cassia, gaultheria, etc. The lower layer will flow off through the long tube as soon as the liquid in the flask or cylinder reaches the height of the curve in the tube, and will continue to flow as long as distillation continues. When the upper layer fills the vessel, the latter must be changed, or if it is provided with two tubes, as shown in Fig. 198, the liquid will pass out through the short tube into another recep-

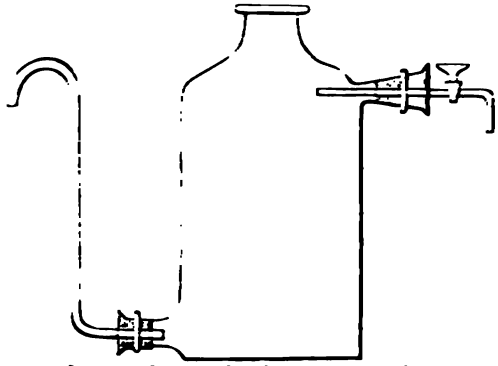
Fig. 197.



Florentine flask for collecting volatile oils.

tacle: thus the two layers of liquid are withdrawn simultaneously almost as fast as separation takes place.

Fig. 198.

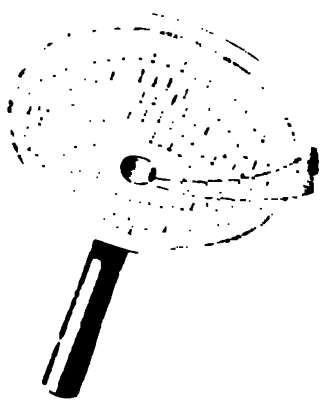


Receiver for volatile oils with two outlets.

Besides distillation, other methods are employed for obtaining volatile oils, such as expression by hand or machine, and extraction by means of suitable solvents: for certain flowers possessing delicate fragrance, such as the violet, heliotrope, mignonette, tuberose, etc., which do not contain volatile oils in appreciable quantities, the treatment with fats by maceration and digestion, or the pneumatic process, is resorted to for obtaining the odorous principles.

Expression is particularly suited for those oils contained in the epidermal cells of the fruit, as in the natural order of Aurantiaceæ, and yields oils of superior quality; the oils of orange and lemon are very sensitive to heat, and hand-pressed oils always command a higher price, on account of their delicate aroma. A special apparatus, known as *écuelle à piquer* (a pricking basin), see Fig. 199, is extensively employed in Southern France; it consists of a tin basin about 8 inches in diameter, studded with numerous 150 short, very pointed brass needles, and provided with a hollow handle. The operator holds the basin in one hand and with the other, while rotating the fruit, he continually presses it against the needle-points, thus rupturing the oil-cells and causing the oil to flow into the handle, whence it is transferred to larger vessels and allowed to separate from any fruit juice with which it has become contaminated. Another method of hand-pressing is

Fig. 199.



practised in Italy, known as the sponge method; the rind of the fruit is separated from the pulp and cut into three or four strips, which are held over a sponge and expressed by convex flexion, whereby the cells are burst and the oil is ejected. When the sponge has become saturated with oil, it is expressed into an earthen vessel. The residual rind is frequently mixed with water and again expressed in linen sacks, to yield a lower grade of oil.

The solvents employed for the extraction of volatile oils are petroleum benzin, ether, carbon disulphide, acetone, etc., solution being effected, in tightly closed apparatus, by means of maceration and percolation. After complete extraction of the volatile oil, the solvent is recovered by distillation at temperatures not affecting the oil, and the residue must then be further purified by rectification. The chief drawback to this method is the possible extraction of other substances besides volatile oils, such as resin, fat, etc., which are sometimes eliminated with great difficulty; hence it is not employed to any great extent.

The process of maceration is confined to the extraction of delicate odors from flowers, and belongs more properly to the art of perfumery than to pharmacy; although the odors are quite marked and persistent, the volatile oil in many flowers is present in such small quantity only that it cannot be recovered by distillation, and in some cases is injured by even moderate heat. Complete absorption of the odorous principle by fats, in the cold, is practised on a large scale in France, where the process is known as *enfleurage;* bland, inodorous fats, such as purified lard, tallow, olive oil, benne oil, and cottonseed oil, being used for the purpose. In the last three cases the flowers are left in contact with the oil, in closed vessels, for some time and then strained. When solid fats are used, they are thinly spread on plates of glass, and then covered with flowers, which are renewed from time to time as long as the fat continues to absorb the odor. The fats, impregnated with the odor of the flowers, are finally scraped from the glass, and constitute the well-known French pomades so extensively employed in the manufacture of fine perfumery. In order to extract the odor, the pomade is repeatedly shaken (washed) with deodorized alcohol and the solution exposed to cold in special cylinders, called crystallizers, whereby all trace of fat is removed.

The pneumatic method consists in passing a current of air into a vessel filled with fresh flowers, whereby the air becomes laden with perfume, and is then passed into another vessel containing fat kept in a fine state of division, so that intimate contact between the air and fat is effected, and thus the odor is transferred to the fat.

Very few volatile oils are of simple composition, and some are even known to contain six or eight distinct bodies. While formerly many arbitrary and erroneous notions were entertained regarding the nature of volatile oils, much light has been shed upon their true character by Wallach and others, during the past ten or twelve

years. Regarding the classification of volatile oils, the plan is still followed of dividing them into simple hydrocarbons or terpenes (containing no oxygen), oxygenated oils, nitrogenated oils, sulphuretted oils, and empyreumatic oils; but the division into elæoptens and stearoptens is no longer maintained. The chemical character and composition of volatile oils will be considered further on, when the student's knowledge of chemistry will better fit him for a proper understanding of the subject.

1. *Carbo-hydrogen Oils, or Terpenes.* The carbo-hydrogen oils are the simplest volatile oils known, being composed of carbon and hydrogen only, and are derived mainly from the natural orders Coniferæ, Leguminosæ, and Piperaceæ. They are divided into hemiterpenes, terpenes, sesquiterpenes, diterpenes, etc. Some of these are frequently found present also in oxygenated oils. The terpenes proper occur in five isomeric forms (having the same centesimal composition, but different properties), known as *pinene, dipentene, limonene, sylvestrene* and *phellandrene;* of these sometimes two or three are found associated in the same oil. As a class, the carbo-hydrogen oils are the least soluble in alcohol and water, and have specific gravities ranging from 0.850 to 0.900. They readily become resinified when exposed to the air, and when left in contact with alcohol and nitric acid gradually absorb water and yield crystallizable compounds. They react violently with iodine, and are converted into a hard resinous mass by nitric acid.

The official members of this class are oil of copaiba, oil of cubeb, oil of erigeron, oil of juniper, oil of savin, and oil of turpentine.

2. *Oxygenated Oils.* These oils, as the name indicates, contain oxygen, and are composed of variable mixtures of terpenes and other bodies, such as alcohols, aldehydes, ethers, acids, ketones, phenols, etc., which can be separated by fractional distillation. Oxygenated oils are widely diffused in plants, but the larger number are derived from the natural orders Umbelliferæ, Labiatæ, Lauraceæ, Myrtaceæ, and Compositæ. The majority of oxygenated oils are soluble in an equal volume of alcohol or glacial acetic acid, and many are soluble in these two liquids in all proportions. They are far more soluble in water than the simple terpenes, and hence are largely used in the preparation of medicated waters. Decreased solubility in alcohol, or in a mixture of alcohol and water, is frequently made a test for adulteration with carbo-hydrogen and other oils.

While the majority of oxygenated oils are lighter than water, a few will sink when dropped into water, the highest specific gravity for volatile oils being found in this class, namely, 1.185 at 15° C. (59° F.). Some, owing to their peculiar chemical composition, will form a solid mass when shaken with an equal volume of concentrated potassa or soda solution, while others show a similar reaction with sodium bisulphite. Upon exposure to low temperatures, some of the oils of this class thicken and even congeal to a solid mass, which fact is utilized as a test for their quality. The value of oxy-

genated oils lies, as a rule, in the oxygenized compounds which they contain, and which are present in the different oils in proportions varying from 1 to 90 per cent. By producing these synthetically, artificial oils, identical with the natural, have been made, of which the official methyl salicylate or artificial oil of wintergreen (identical also with the natural oil of sweet birch) is an example. The Pharmacopœia recognizes a single concrete volatile oil, camphor, which can be appropriately classed among the oxygenated oils, since its chemical composition shows it to be a pure oxidized hydrocarbon.

The official oxygenated oils are those of anise, bergamot, betula, cajeput, caraway, cloves, chenopodium, cinnamon, coriander, eucalyptus, fennel, gaultheria, hedeoma, lavender flowers, lemon, orange flowers, orange peel, peppermint, spearmint, myrcia, nutmeg, pimenta, rose, rosemary, santal, sassafras, and thyme. Of these, the oils of bergamot, orange peel, and orange flower consist almost entirely of limonene, one of the isomeric terpenes, containing less than 3 per cent. of undetermined oxygenated bodies.

3. *Nitrogenated Oils.* Some plants do not produce volatile oils in nature, but contain certain principles which, in the presence of water, react upon each other, causing the formation of new compounds, one of which is a volatile oil; such is the case with certain plants belonging to the natural order Rosaceæ, sub-order Amygdalæ. The volatile oil, when absolutely pure, contains no nitrogen, but the name nitrogenated oils has been given to this class because in their formation they are always accompanied by a nitrogenized substance, hydrocyanic acid, which is present in variable proportion and which lends to the oils their poisonous character. The only official nitrogenated oil is the oil of bitter almond, which is prepared by mixing freshly powdered bitter almonds with the residue left after expressing the fixed oil from bitter and sweet almonds, adding water, and distilling at a moderate heat. The specific gravity of the oil ranges from 1.060 to 1.070 at 15° C. (59° F.), and that of the purified oil is about 1.045. The oil is sometimes adulterated with nitrobenzene or artificial oil made from toluene. Bitter almonds, like peach and cherry seeds, contain both the albuminous ferment and the peculiar compound, amygdalin, necessary for the reaction, while sweet almonds contain only the ferment, and hence will yield no volatile oil unless mixed with the bitter variety. The hydrocyanic acid present in oil of bitter almond sometimes amounts to as much as 6 or 7 per cent., and may be removed by shaking the oil with ferrous chloride and lime-water and then rectifying by distillation. Oil of bitter almond is soluble in 300 parts of water and in all proportions of alcohol.

4. *Sulphuretted Oils.* Like the preceding class, these oils are the result of fermentative action, in which the living plant takes no part except to provide the necessary active principles for the subsequent reaction in the presence of water. Sulphur is present in the oils, combined with certain organic radicles, in the form of sulphide or sulphocyanate. Nearly all the oils of this class are obtained from

members of the natural order Cruciferæ. The Pharmacopœia recognizes but one sulphuretted oil, namely, the volatile oil of mustard, made from black mustard seed, which has a specific gravity varying from 1.018 to 1.029 at 15° C. (59° F.). When shaken with alcohol and ammonia water and slightly warmed, the oil deposits crystals of thiosinamine: 3 Gm. of oil should yield not less than 3.25 Gm. nor more than 3.5 Gm. of such crystals.

5. *Empyreumatic Oils.* Among the products of destructive distillation are certain volatile oils, which are characterized by a peculiar tarry odor, an acid reaction and a somewhat bitter taste. They are lighter than water, sparingly soluble in that liquid, but readily soluble in alcohol. Oil of cade and oil of tar are the only empyreumatic oils recognized in the Pharmacopœia; the former is obtained by the dry distillation of the wood of the prickly cedar (juniperus oxycedrus) and the latter by distillation of tar.

PART II.

PRACTICAL PHARMACY.

THE study of practical pharmacy involves both galenical and extemporaneous pharmacy, the former pertaining to the various preparations of drugs, the latter to the many operations of the dispensing counter. The different classes of plant products used in medicine, as well as the various methods of solution and separation, have been considered in previous chapters; the numerous preparations of drugs will be treated after a plan which, for a number of years, has proven satisfactory to students, and although not based on a strictly symmetrical arrangement, is probably in keeping with the advance made by them in other branches of study up to this point.

The official preparations may be divided into those of a strictly pharmaceutical character and those involving chemical action; the latter class will be considered under the head of pharmaceutical chemistry, where the preparations of each element or compound will be grouped together.

The galenical preparations of the Pharmacopœia may be classified as follows: 1, Waters; 2, Solutions or Liquors; 3, Decoctions and Infusions; 4, Syrups; 5, Mucilages, Honeys, and Glycerites; 6, Elixirs; 7, Spirits; 8, Tinctures; 9, Wines and Vinegars; 10, Fluid Extracts; 11, Extracts; 12, Oleoresins and Resins; 13, Collodions; 14, Emulsions; 15, Mixtures; 16, Pills; 17, Lozenges and Confections; 18, Powders and Triturations; 19, Granular Effervescent Salts; 20, Cerates and Ointments; 21, Liniments and Oleates; 22, Plasters and Suppositories.

The operations of the dispensing counter are intimately associated with the various preparations of drugs officially recognized, and, instead of treating them separately under a special head, it is thought most convenient to consider them in connection with some of the subdivisions named above, particularly as eight classes of the official galenical preparations require remarks and explanations, which apply equally to the details of dispensing pharmacy. Certain forms of administering medicines, not as yet recognized in the Pharmacopœia, but which, of late years, have come into use extensively, such as Compressed Tablets, Tablet Triturates, Hypodermic Tablets, Medicated Disks, etc., may be looked upon as modifications of the official class of lozenges and studied in connection with these.

CHAPTER XIII.

THE OFFICIAL WATERS.

THE official waters include common and distilled water, as well as those known as medicated waters; the latter are all solutions of volatile substances, and were it not for this pharmacopœial classification, four of them might be considered as more appropriately belonging to the class of liquors or solutions proper, instead of medicated waters, namely, *aqua ammoniæ, aqua ammoniæ fortior, aqua chlori*, and *aqua hydrogenii dioxidi.*

The U. S. Pharmacopœia directs three different methods for the preparation of medicated waters; namely, by simple agitation of the medicinal ingredient with cold water, by trituration of essential oils with precipitated calcium phosphate and water, and by distillation. In England and Germany the second method is not practised, the pharmacopœias of both countries directing all aromatic waters to be made by distillation. Another excellent method for making aromatic waters is that known as the hot-water method; the volatile oil may either be dropped upon shredded filter paper, and this shaken with hot water in a strong bottle for some time, or the oil may be dropped into a stone jug and run around the sides, after which the hot water is added and agitated until cold; in either case the finished solution is passed through a paper filter, and will be found of excellent quality.

The most important of the official waters is undoubtedly distilled water, because it is intended to be absolutely free from impurities, inorganic as well as organic, and is the only kind that should be used in making aromatic waters. River water and most spring waters contain in solution varying quantities of mineral compounds, and frequently carbon dioxide and organic matter, which render the water unfit for many pharmaceutical purposes; boiling and subsequent filtration through sand and charcoal will improve the water, but do not remove the salts held in solution, which if present in appreciable quantity will cause precipitation if silver nitrate or lead acetate be dissolved in the water. The so-called hardness of water may be due to the presence of calcium sulphate, and is then known as permanent hardness, or it may be due to calcium carbonate held in solution by an excess of carbon dioxide, which is always the case with spring water coming from limestone districts; boiling such water expels the excessive carbon dioxide, causing the lime-salt to be precipitated, whereby it is rendered soft. The directions of the Pharmacopœia to reject the first 10 per cent. of the distillate and to collect only 80 per cent. for use, are for the purpose of getting rid of the

gases and volatile compounds always present in water, and to avoid the decomposition-products from ammonia compounds and organic matter, with which the last portions of water in the still are apt to be contaminated.

The condensed steam from boiler pipes is frequently sold as distilled water, but, unless collected with care, will often be found very unsatisfactory and not up to the requirements of the Pharmacopœia. In the manufacture of distilled water all contact with iron and lead should be avoided, and either glass or pure tin apparatus used, especially for the condensation of the vapors. The occasional appearance of confervæ (microscopic plants) in distilled water is due to the presence of minute spores derived from the air, and may be prevented by keeping it in vessels so arranged that the air can enter only after having passed through a layer of cotton. Aromatic waters made with distilled water are subject to the same difficulties. The addition of alcohol, which has been recommended as a preservative measure, is inadmissible, because a small quantity would predispose the water to acetous fermentation (souring), as has been proven, and larger quantities might interfere therapeutically.

The following classification of the official waters shows, at a glance, their strength and mode of preparation:

OFFICIAL WATERS MADE BY AGITATING THE MEDICINAL INGREDIENT WITH COLD WATER.

Official Name.	Strength.
Aqua Amygdalæ Amaræ	0.1 per cent. by volume of Oil of Bitter Almond
Aqua Aurantii Florum	50 per cent. of stronger Orange Flower Water.
Aqua Chloroformi	Saturated. About 0.5 per cent. by volume of Chloroform.
Aqua Creosoti	1 per cent. by volume of Creosote.
Aqua Hydrogenii Dioxidi	About 3 per cent. by weight of pure Hydrogen Dioxide, or 10 volumes of available Oxygen.
Aqua Rosæ	50 per cent. of stronger Rose Water.

Bitter almond water is likely to contain variable proportions of hydrocyanic acid, as this acid is usually present in the commercial oil; it is a weak and very uncertain preparation. The German Pharmacopœia directs that bitter almond water shall be made by distillation and shall contain 0.1 per cent. of absolute hydrocyanic acid; this corresponds in strength to the distilled cherry-laurel water of the British Pharmacopœia.

OFFICIAL WATERS MADE BY PASSING GASES THROUGH WATER.

Official Name.	Strength.
Aqua Ammoniæ	10 per cent. by weight of gaseous Ammonia.
Aqua Ammoniæ Fortior	28 per cent. by weight of gaseous Ammonia.
Aqua Chlori	0.4 per cent. by weight of gaseous Chlorine.

Chlorine water is very prone to change; it should always be kept in well-filled bottles, in a cool, dark place, as air and light hasten deterioration.

OFFICIAL WATERS MADE BY TRITURATING THE MEDICINAL INGREDIENT WITH PRECIPITATED CALCIUM PHOSPHATE AND THEN MIXING WITH COLD WATER AND FILTERING.

Official Name.	Strength.
Aqua Anisi	0.2 per cent. by volume of Oil of Anise.
Aqua Camphoræ	8 Gm. of Camphor in 1000 Cc.
Aqua Cinnamomi	0.2 per cent. by volume of Oil of Cinnamon.
Aqua Fœniculi	0.2 per cent. by volume of Oil of Fennel.
Aqua Menthæ Piperitæ	0.2 per cent. by volume of Oil of Peppermint.
Aqua Menthæ Viridis	0.2 per cent. by volume of Oil of Spearmint.

With the exception of camphor water, this whole class is prepared by triturating the oil with twice its weight of calcium phosphate, for the purpose of minute subdivision, then adding gradually, under constant trituration, sufficient distilled water to make the desired volume, and finally filtering the mixture through paper. In the case of camphor water, 8 Gm. of camphor are triturated with 5 Cc. of alcohol and 5 Gm. of calcium phosphate, after which the preparation is finished like the others.

Other absorbent powders have been used from time to time to facilitate the division of the oil, such as magnesium carbonate, prepared chalk, purified talcum, etc.; but, of all, magnesium carbonate is the least desirable, from the fact that a minute quantity of the salt is always dissolved, and, in a few cases, compounds with the acids naturally present in some oils are formed; cinnamon water made with magnesium carbonate is always colored yellowish, whereas, if distilled or made with calcium phosphate or purified talcum, a colorless solution is obtained. The plan of distributing the volatile oil over purified cotton and then bringing it into aqueous solution, by slow percolation with distilled water, which was officially directed in the Pharmacopœia of 1880, yields aromatic waters of fine flavor, but is objectionable, on account of the possible bad effects due to prolonged contact of the oils with the fingers of the operator.

OFFICIAL WATERS MADE BY DISTILLATION.

Official Name.	Strength.
Aqua Aurantii Florum Fortior	Saturated.
Aqua Destillata	Absolutely pure.
Aqua Rosæ Fortior	Saturated.

Aromatic waters made by distillation, in many instances, possess a more agreeable flavor than the aqueous solution of the corresponding volatile oils, which is probably due to the fact that, besides the volatile oil, other volatile compounds, such as acids or ethers, are present in the drug, and, passing over with the steam, remain dissolved in the condensed water. In distilling aromatic waters over a naked fire, care should be taken to prevent the material from being scorched, which can be obviated by placing the drug either upon a diaphragm or in a perforated vessel or wire cage, and then suspending this in the water. A peculiar odor is observed in some waters immediately after they have been distilled and condensed in tin vessels, but not

when glass vessels have been used; if the waters be exposed to the air in loosely stoppered vessels, for a few days, this still-odor disappears and the natural odor of the water becomes apparent.

The *stronger* orange flower and rose waters are obtained, on a large scale, often as by-products in the distillation of the respective oils; in commerce they are distinguished as of *triple* or *quadruple* strength. In order to produce a saturated solution of the oil, recourse is had to

FIG. 200.

The Curran Water Still.

A is a tin-lined copper boiler. C is a galvanized jacket for supporting the boiler over the gas burners, and is attachable at B, D; it is also intended to act as a flue to utilize the heat from the gas burners on the sides of the boiler. H is a screw cover removable for filling or cleansing the boiler. F is the vapor pipe from the boiler to the condensing coil, P, in the galvanized iron condensing tank, E, which is provided with an inlet for cold water at T, and an outlet for the warm water at I. At G is a union for connecting the vapor pipe with the condensing coil. S is the outlet for the condensed water, and X is the receiving vessel. J is a perforated ring resting on the jacket, and K are vent holes in the ring, through which the exhausted gases pass off. O is a removable cover for cleansing out the condensing tank. R is a faucet for drawing off the water from the condensing tank. L, L, L are the gas burners, and N the iron frame supporting the apparatus and burners. M is a gas cock for regulating the supply of gas to the burners.

the process of *cohobation* or redistillation, which consists in distilling the same water two or three times with fresh portions of the flowers. In some factories, saturated orange flower and rose waters are obtained, not as by-products, but direct from the flowers, by distilling them with relatively small quantities of water; thus triple strength water is distilled by using three parts of the flowers to one of water, etc. According to Schimmel & Co., of Leipzig, Germany (extensive distillers of volatile oils and aromatic waters), sextuple rose water represents the highest obtainable concentration, and rose water prepared from more than six times its weight in roses will not retain the whole of its oil in solution, at ordinary temperature.

For the preparation of distilled water a special apparatus has been put upon the market, which is said, by those who have used it, to yield an exceptionally pure water and in considerably larger quantity than is usually expected from a still of like size. The apparatus, which is illustrated in Fig. 200, is known as the Curran Water Still, and can be used anywhere if gas and constant water supply be available.

The tin-lined copper boiler has a capacity of five gallons, and from it, four and a half gallons of distilled water can be obtained in about two and a half hours; this allows the first quart of distillate, carrying with it all volatile matter, to be rejected, and also retains a quart of water in the boiler. The rapid vaporization of the water in the boiler is effected by means of four rose burners consuming jointly about twenty-five feet of gas per hour, the generated heat being all utilized on the bottom and sides of the boiler, which is surrounded by a galvanized iron jacket, as shown in the cut. The vapor-pipes passing from the boiler, and the condensing coil, are both heavily lined with pure block tin, thus avoiding contact of the water with any other metal. There is no pressure on any part of the apparatus, the vapor being condensed as fast as generated and the distillate passing rapidly into the receiving vessel. Larger sizes of the Curran Water Still are made for use with gas or coal, delivering, according to the manufacturer's statements, which they guarantee, from four to ten gallons of distilled water per hour.

CHAPTER XIV.

THE OFFICIAL SOLUTIONS OR LIQUORS.

THE term *Liquor* is applied in the Pharmacopœia to all aqueous solutions of non-volatile substances. In Europe the name is applied in a less restricted sense, and in England it is not even confined to aqueous solutions. Twenty-four liquors are officially recognized, and of these, eight are made by simple solution of the medicinal agent in water, fifteen involve chemical action in their preparation, and for one the Pharmacopœia gives no process of manufacture. This solution—the liquor sodii silicatis—is made on a large scale by manufacturers, being used extensively in the arts, and for medicinal use should be of the density officially prescribed. For two of the solutions—those of potassa and soda—double formulas are given: one a simple solution, the other a more tedious chemical process; the former plan is usually followed by pharmacists, while the latter is preferred by manufacturers. The official liquors may therefore be conveniently divided into two groups, as follows:

1. *Simple Solutions.* The active ingredient is added directly to the water.

Official Name.	Strength.
Liquor Acidi Arsenosi	1 Gm. Arsenous Acid, 5 Cc. Diluted Hydrochloric Acid. in 100 Cc.
Liquor Arseni et Hydrargyri Iodidi (Donovan's Solution)	1 Gm. Arsenic Iodide, 1 Gm. Red Mercuric Iodide. in 100 Cc.
Liquor Calcis (Lime Water) . .	Saturated; contains about 0.17 per cent. of Calcium Hydroxide at 15° C. (59° F.), but the percentage decreases as the temperature rises.
Liquor Iodi Compositus (Lugol's Solution)	5 per cent. of Iodine and 10 per cent. of Potassium Iodide.
Liquor Plumbi Subacetatis Dilutus Lead Water)	3 per cent. by volume of Solution of Lead Subacetate (Goulard's Extract).
Liquor Potassæ	About 5 per cent. of Potassa (Potassium Hydroxide).
Liquor Sodæ	About 5 per cent. of Soda (Sodium Hydroxide).
Liquor Sodii Arsenatis . . .	1 Gm. anhydrous Sodium Arsenate in 100 Cc

2. *Chemical Solutions.* The active ingredient is formed in the process of manufacture, as the result of chemical action.

Official Name.	Strength.
Liquor Ammonii Acetatis (Spirit of Mindererus). Made from ammonium carbonate and diluted acetic acid.	About 7 per cent. of Ammonium Acetate.
Liquor Ferri Acetatis. Made from ferric hydroxide, glacial acetic acid, and water	About 3 per cent. of anhydrous Ferric Acetate.
Liquor Ferri Chloridi. Made from iron wire, hydrochloric and nitric acids, and water.	About 37.8 per cent. of anhydrous Ferric Chloride.
Liquor Ferri Citratis. Made from ferric hydroxide, citric acid, and water.	About 7.5 per cent. of metallic Iron.
Liquor Ferri et Ammonii Acetatis. (Basham's Mixture). A mixture of tincture of ferric chloride, spirit of Mindererus, diluted acetic acid, aromatic elixir, glycerin, and water.	About 0.1 per cent. of metallic Iron.
Liquor Ferri Nitratis. Made from ferric hydroxide, nitric acid, and water.	About 6.2 per cent. of anhydrous Ferric Nitrate.
Liquor Ferri Subsulphatis (Monsel's Solution). Made from ferrous sulphate, nitric and sulphuric acids, and water.	About 13.6 per cent. of metallic Iron.
Liquor Ferri Tersulphatis. Made like the preceding, except that more sulphuric acid is used.	About 28.7 per cent. of Ferric Sulphate.
Liquor Hydrargyri Nitratis. Made from red mercuric oxide, nitric acid, and water.	About 60 per cent. of Mercuric Nitrate.
Liquor Magnesii Citratis. Made from magnesium carbonate, citric acid, syrup of citric acid, potassium bicarbonate, and water.	About 6.25 Gm. of Magnesia in 360 Cc.
Liquor Plumbi Subacetatis. Made from lead acetate, lead oxide, and water.	About 25 per cent. of Lead Subacetate.
Liquor Potassæ. Made from potassium bicarbonate, lime, and water.	About 5 per cent. of Potassa (Potassium Hydroxide).
Liquor Potassii Arsenitis (Fowler's Solution). Made from arsenous acid, potassium carbonate, compound tincture of lavender, and water.	1 Gm. Arsenous Acid in 100 Cc.
Liquor Potassii Citratis (Mistura Potassii Citratis). Made from potassium bicarbonate, citric acid, and water.	About 9 per cent. of anhydrous Potassium Citrate.
Liquor Sodæ. Made from sodium carbonate, lime, and water	About 5 per cent. of Soda (Sodium Hydroxide).
Liquor Sodæ Chlorinatæ (Labarraque's Solution). Made from sodium carbonate, chlorinated lime, and water	At least 2.6 per cent. of available Chlorine
Liquor Sodii Silicatis. Made from quartz, sodium hydroxide, and water.	About 33 per cent. of Sodium Silicate (a mixture of tri- and tetra-silicate).
Liquor Zinci Chloridi. Made from granulated zinc, hydrochloric and nitric acids, and water	About 50 per cent. of Zinc Chloride.

CHAPTER XV.

DECOCTIONS AND INFUSIONS.

Decoctions.

DECOCTIONS are aqueous solutions of the active principles of vegetable drugs, prepared at a boiling temperature. This process is obviously not adapted to drugs containing volatile principles, or those whose activity depends upon resinous constituents. Drugs of a very close texture, or the active virtues of which cannot be exhausted below the temperature of boiling water, are best suited for the process of decoction. In former years, decoctions were extensively employed, and frequently made by using a large quantity of water and boiling it down, in open vessels, to one-half, or even to a less amount. This method offered no obvious advantage, and, in fact, often proved decidedly disadvantageous, on account of the deleterious effect upon the constituents of the drug by long exposure to air and heat. In this country at least, decoctions have almost entirely disappeared from the physician's armamentarium, and the pharmacist is but rarely called upon to prepare them; the U. S. Pharmacopœia, since 1880, has officially recognized only two of these preparations—namely, decoction of cetraria and compound decoction of sarsaparilla.

Decoctions as well as infusions must always be prepared extemporaneously, since they will readily deteriorate, on account of the perishable matter in solution and the absence of alcohol or other preservative.

The Pharmacopœia gives the following general directions for preparing decoctions whenever a special strength is not indicated by the physician: Put 50 Gm. of the substance, coarsely comminuted, into a suitable vessel provided with a cover; pour upon it 1000 Cc. of cold water, cover well, and boil for fifteen minutes; then let it cool to about 40° C. (104° F.), strain the liquid, and pass through the strainer enough cold water to make the product measure 1000 Cc.

The use of cold water, to begin with, insures the complete extraction from the drug of all its soluble principles, by the gradually heated water, the albuminous matter being subsequently coagulated as the heat is increased to near the boiling-point. If, on the other hand, the drug be at once immersed in boiling water, the albumen contained in cells would be coagulated, and thus seriously interfere with the extraction of the other constituents. In preparing compound decoctions, all the drugs may be added to the cold water, with the exception of those which, like senna, are injured by long-

continued heat, or which contain aromatic or other volatile principles; such should be added when the decoction is ready to be removed from the fire or steam-bath, and allowed to digest until it is sufficiently cooled for straining. The material should in all cases be cut or bruised, the degree of fineness depending upon the nature of the tissue Woody drugs may be reduced to a moderately fine powder; leaves, however, and other drugs consisting mainly of loose parenchyma, are better used in the form of a moderately coarse or very coarse powder.

Unless the liquid is to be considerably boiled down, decoctions are best prepared in a vessel provided with a cover, which may be loosely put on until the boiling is completed, when the vessel should be well closed, particularly if additions have been made at the close of boiling. Porcelain is undoubtedly the best material for vessels used for preparing decoctions, since it is not acted upon by the various vegetable principles; for similar reasons, glass flasks will answer a useful purpose in making small quantities of these preparations. As a rule, it is best to avoid metallic vessels, except when made of block tin and used in connection with a steam bath. As many drugs contain tannin, vessels made of iron are not adapted for preparing their decoctions, and the usually imperfect covering of galvanized or tinned sheet iron renders the vessels lined with such material but little better suited for this purpose, and still inferior to properly enamelled iron vessels.

As a rule, decoctions should be allowed to cool to below 40° C. (104° F.) before they are strained; principles which are soluble only in hot water are then mostly precipitated, and removed without, in most cases, weakening the medicinal effects of the preparations; but, even with this precaution, the strained liquid may become unsightly in appearance by the further deposition, on cooling, of apotheme or matter soluble only in hot water. In such cases the pharmacist should be guided by the directions of the Pharmacopœia or the intentions of the physician, and not sacrifice effect to elegance.

Official Decoctions.

Decoction of Cetraria is made by first macerating the cetraria with cold water, for half an hour, in order to remove a portion of the bitter principle present; this liquid is rejected, after which the drug is boiled with fresh water, for half an hour. Each Cc. represents 0.050 Gm. of cetraria.

In compound decoction of Sarsaparilla, the sarsaparilla and guaiacum wood are directed to be boiled with water, for half an hour, after which the sassafras, liquorice root, and mezereum are added, and the whole is macerated without further heat in a well-covered vessel. Each Cc. represents 0.10 Gm. of sarsaparilla, 0.020 Gm. each of guaiacum wood, sassafras, and glycyrrhiza, and 0.010 Gm. of mezereum.

In the British Pharmacopœia, thirteen decoctions are recognized, all of which are directed to be made with distilled water, and, in the majority of the formulas, boiling is continued for only ten minutes.

The German Pharmacopœia directs decoctions to be made of the strength of ten per cent. when not otherwise specified, by keeping the mixture of drug and cold water, for half an hour, in a bath of steam arising from boiling water, and then expressing while warm. Two preparations termed *decoctions*, of althæa and of flaxseed, are prepared cold by maceration for half an hour and subsequent gentle expression; they belong more properly under the head of *mucilages*.

Infusions.

Infusions are aqueous solutions of the soluble principles of vegetable or animal drugs, obtained by maceration or digestion in hot or cold water, and differ from decoctions only in the lower degree of heat employed in their preparation. This process is particularly suitable for substances containing volatile or other principles which would be dissipated or injured by boiling. A convenient apparatus, well adapted for making these preparations, is Squire's infusion-pot, Fig. 201. This consists of the jar, A, with a projecting ledge near

Fig. 201.

Squire's infusion-pot.

the top, which supports a strainer, B or D, containing the material to be exhausted; the jar is closed by a well-fitting cover, C. The advantages of this contrivance are, that the material is exhausted by circulatory displacement—the liquid, as it becomes charged with the soluble ingredients, descending to the bottom, giving place to fresh portions of less saturated menstruum—and that no further straining is required if care has been taken not to use too fine a powder.

Drugs are best adapted for exhaustion with water when cut into thin slices by a suitable knife, so that they may be easily permeated by the liquid; if cutting be inadmissible, they should be bruised to a coarse powder. Ligneous drugs, however, should be in a fine

or moderately fine powder, which is also best adapted for most of those infusions which may be made by percolation.

Wherever possible, infusions should be made in porcelain or porcelain-lined vessels, to avoid contact with metal.

The U. S. Pharmacopœia has adopted the plan of ordering all infusions, unless otherwise directed by the physician, with the exception of four specially enumerated, to be made of 1 part of material to 20 parts of infusion, according to the following directions: "An ordinary infusion, the strength of which is not directed by the physician nor specified by the Pharmacopœia, shall be prepared by the following formula: Take of the substance, coarsely comminuted, 50 Gm.; boiling water, 1000 Cc.; water a sufficient quantity to make 1000 Cc. Put the substance into a suitable vessel provided with a cover, pour upon it the boiling water, cover the vessel tightly, and let it stand for one-half hour. Then strain, and pass enough water through the strainer to make the infusion measure 1000 Cc.

The Pharmacopœia omits to direct the expression of the drug after infusion, but it is evident that bulky herbs and flowers, which are best adapted to this process, would retain a considerable proportion of the liquid, which cannot be washed out simply by passing water through the strainer to make up the deficiency in volume.

Both in the cases of decoctions and infusions, the Pharmacopœia requires that, when made of energetic or powerful substances, the physician shall specify the desired strength.

Four infusions are officially recognized in the Pharmacopœia, two prepared cold, by percolation, and two by maceration with hot water; the time directed for the latter method is not specified, maceration being continued until the liquid is cold.

The strength of infusions of the German Pharmacopœia is double that of our own, but the general directions given for their preparation are nearly identical with the above, from which they differ only in this, that the mixture of drug and boiling water is heated for five minutes in a vapor bath of boiling water, occasionally stirred, allowed to cool, and strained.

Official Infusions.

MADE BY PERCOLATION.

Name	Strength.
Infusum Cinchonæ	6.0 Gm. of Cinchona; 1.0 Cc. of Aromatic Sulphuric Acid — In 100 Cc.
Infusum Pruni Virginianæ	4.0 Gm. of Wild Cherry in 100 Cc.

Both infusions, if carefully prepared, are efficient preparations of the drugs from which they are made; the former will contain all the alkaloids of cinchona, in solution as sulphates, and the latter, any hydrocyanic acid generated in the bark by the aid of water.

MADE BY HOT MACERATION.

Name	Strength.	
Infusum Digitalis	1.5 Gm. of Digitalis in 100 Cc.	
Infusum Sennæ Compositum (Black Draught)	6.0 Gm. of Senna 12.0 Gm. of Manna 12.0 Gm. of Magnesium Sulphate 2.0 Gm. of Fennel	In 100 Cc.

Infusion of digitalis is pleasantly flavored with cinnamon water, and contains 10 per cent. by volume of alcohol, hence it will keep for a few days, particularly in a cool place.

$C_{12}H_{22}O_{11} + H_2O$ diminish about 24%

CHAPTER XVI.

SYRUPS.

In pharmacy the term syrup is applied to concentrated solutions of sugar, the solvent being either water or an aqueous, acetous, or hydro-alcoholic solution of some medicinal or aromatic principle. The Pharmacopœia applies the name *syrupus* or *syrup* to a nearly saturated solution of sugar in water; in practice this solution is usually termed *simple syrup* as a mark of distinction. Syrups are an old and favorite form of administering medicines, partly on account of the sweet taste, and partly because sugar is used as a preservative for otherwise unstable vegetable solutions, in place of alcohol, which is often contra-indicated in disease. The sugar used in making syrups should be of the best quality obtainable, as upon it depend the character and stability of the finished syrup. The Pharmacopœia describes sugar as occurring in white, hard, crystalline granules, of purely sweet taste, which corresponds to the best commercial varieties known as granulated and cut loaf sugar; in order to overcome the yellowish cast of sugar, refiners frequently add ultramarine, Prussian blue, etc., which, to some extent, will pass even through paper filters and finally deposit in the syrup containers.

Sugar is soluble in half its weight of water at 15° C. (59° F.), and a saturated solution thus prepared has the specific gravity 1.345; it is also soluble in 175 times its weight of official alcohol. Large quantities of sugar dissolved in water very materially increase the bulk of the liquid, a fact which must always be borne in mind in the preparation of syrups; practically, two-thirds of the weight of sugar will equal its bulk in fluid measure, or, in other words, 750 Gm. of sugar when dissolved in water will increase its bulk about 500 Cc. The proper proportion of sugar to menstruum is of great importance, as upon it depends the stability of the syrup. Should the sugar be deficient in quantity, it could not efficiently protect the other organic principles in the syrup, and the latter would be liable to ferment. On the other hand, if too much sugar be dissolved by the aid of heat, the excess will crystallize after cooling and dispose an additional quantity to separate in like manner, thus leaving the syrup weaker in sugar than it should be and subject to similar alterations as if an insufficient quantity of sugar had been used.

Preparation. In the preparation of syrups, solution of the sugar may be effected by one of the following methods: Agitation of sugar and solvent without heat, cold percolation of the sugar with the solvent, gentle heating of the sugar and solvent, or heating the mix-

ture of sugar and solvent to the boiling-point. The application of heat in the manufacture of syrups should be avoided as far as possible, especially a boiling temperature, partly to prevent the loss of volatile constituents and partly to guard against any change in the character of the sugar, which, under the influence of heat and particularly with acid liquids, is converted into inverted sugar, resembling glucose, and thereby predisposed to fermentation; moreover, the use of heat, in open vessels, causes evaporation of a part of the solvent, which, if not restored, produces a supersaturated solution with the attending evil of crystallization referred to above.

The preparation of syrups without heat is a feature of American pharmacy, both the British and German Pharmacopœias directing the use of heat in every instance. By some authorities it is claimed that syrups made with heat are more permanent than those made cold; this claim is not supported by experience in this country. For all syrups containing volatile principles or such as may be changed by heat, the cold process is positively advantageous, and if pure sugar be used, such syrups keep admirably.

The process of cold percolation of sugar with the solvent was first suggested by L. Orinsky in 1871, and is now largely recommended in the Pharmacopœia; the process is of decided advantage whenever the syrup is to be prepared without heat, although it requires a little care in its management so as to insure perfect solution and a clear percolate. A cylindrical, slightly tapering percolator is best adapted for the purpose. A clean soft piece of sponge is placed, with moderate pressure, in the neck of the percolator (if too tightly compressed the viscid liquid will not pass through, and if too loose the liquid passes too rapidily and not clear), upon it is poured the sugar in granular form and properly levelled and shaken down by tapping the sides of the percolator, after which a diaphragm of filter paper is laid on the surface and the solvent carefully poured on with the aid of a guiding rod. If the sponge or a tuft of absorbent cotton has been properly adjusted, the solution will be perfectly clear and transparent and pass out in drops only, all the sugar being taken up before the end of the process; but if the liquid passes too rapidly, or if it be turbid, it must be poured back into the percolator until the defect is remedied. Some objections have been made to this process, such as the time necessary for perfect solution of the sugar, and the fact that albuminous principles liable to induce fermentation are best removed by heat; but it must be borne in mind that cold percolation requires very little attention after it has once been started, can be allowed to go on during the night, and does away with the necessity of subsequent filtration; the evil tendency of nitrogenized principles in the solvent may be overcome by the use of weak alcohol and glycerin, as is directed in many of the official formulas.

In the case of some syrups, where the viscid character of the solvent precludes rapid solution of the sugar, or when the syrup is wanted in a hurry, a moderate heat may be employed to facilitate

solution, by putting the sugar and solvent into a strong bottle one and a half times as large as the required volume of syrup, and, after securely corking, keeping it in a heated water-bath at about 50° C. (122° F.), and frequently agitating until perfect solution is effected; all loss of volatile principles is avoided by keeping the bottle well corked. Whenever the solvent contains latent ferments or a large proportion of albuminous matter, heating to the boiling-point is necessary, in order to render such principles harmless, as in the case of syrups prepared from fruit juices; but the heat should not be continued beyond the boiling-point, to avoid a change in the sugar.

When large quantities of syrup are to be made with heat, the mixture of sugar and solvent is placed in a porcelain-lined or well-tinned kettle and heated over a direct fire or on a steam-bath, until the sugar is dissolved; it is then strained and water added to make up the desired volume.

PRESERVATION. Syrups are best preserved in completely filled bottles, in a cool place, and will keep unaltered, if properly prepared, for a long time; the addition of preservatives, such as salicylic or boric acid, calcium sulphite, ether, etc., is unnecessary, and in fact, objectionable, and such syrups as cannot be kept with ordinary care should be made in small quantity only. When syrups have undergone fermentation they are no longer fit for use, and even if the attempt be made to restore them by boiling, they are likely soon to spoil again, owing to the decreased proportion of sugar left in solution; the best and safest plan is to throw them away. Finished syrups should always be put into perfectly *clean and dry* bottles (if made so by heat, after they have become cold), so as to avoid dilution and possible contamination with fermentation germs, which are likely to lurk in imperfectly cleaned bottles. Bottles from which syrups have been dispensed should be thoroughly washed with weak lye and afterward with water, and then dried before they are refilled.

All syrups, whether made by cold or hot process (except cold percolation), require straining through flannel to remove particles of dust and dirt, and, in the case of colorless or light-colored syrups, their appearance will be greatly improved by filtering them, under cover, through paper or a pledget of cotton.

The Official Syrups.

The U. S. Pharmacopœia recognizes thirty-two syrups, which may be conveniently divided into flavoring and medicated syrups; of these, twenty-five are directed to be made *without heat*, three are raised to boiling heat, and in the remaining four the sugar is to be dissolved with a gentle heat. Of the twenty-five syrups made without heat, ten are merely mixtures of simple syrup and medicating liquids.

A. Flavoring Syrups.

1. *Syrupus.* Official simple syrup contains 64.54 per cent. by weight of sugar, each Cc. representing 0.85 Gm.; it should be made with distilled water so as to produce a solution of crystalline clearness, and if heat be employed, the syrup should be passed through a small, dry strainer, which is then washed with sufficient distilled water used for rinsing the vessel, to bring the volume up to the required quantity. Simple syrup should be made and preserved with care. One pound measures very nearly twelve fluidounces.

2. *Syrupus Acidi Citrici.* Syrup of citric acid is made by mixing spirit of lemon and a solution of citric acid with simple syrup; it is an excellent substitute for lemon syrup, being more stable and of uniform acidity. It is of pleasant flavor and slightly opalescent, each Cc. containing 0.010 Gm. of citric acid. Unfortunately syrup of citric acid, when kept on hand for some time, acquires a terebinthinate odor; it should therefore be made in small quantities.

3. *Syrupus Amygdalæ.* Syrup of almond, or orgeat syrup, should always be made from blanched almonds, so as to be as free from color as possible; blanching of almonds consists in macerating them in hot water until the yellow episperm, or skin, loosens and can be removed by pressing between the fingers. The blanched almonds are beaten into a smooth paste with sugar and water, to which syrup and orange-flower water are gradually added; sugar is then dissolved in the strained liquid. Syrup of almond (also known in Europe as *syrupus emulsivus*) is whitish and opaque, and, when added to water yields a milk-like mixture; it spoils readily unless kept in a cool place, in well-stoppered, completely-filled bottles.

4. *Syrupus Aurantii.* Syrup of orange is made from a concentrated tincture of the *fresh, outer* orange peel, which is mixed with calcium phosphate, sugar, and water, and then filtered; the remainder of the sugar is dissolved in the filtrate. The finished product contains 10 per cent. of alcohol, and possesses an agreeable aroma. Syrup of orange should never be made by mixing fluid extract of orange peel with syrup, as practised by some pharmacists; when so made it is more or less bitter, is without the fine orange flavor, and turns liquids containing iron preparations dark, on account of the tannin in the peel, which is not the case with the official syrup.

5. *Syrupus Aurantii Florum.* Syrup of orange flowers contains the same proportion of sugar as simple syrup; it is made without the aid of heat, most conveniently by percolation.

6. *Syrupus Rubi Idæi.* Syrup of raspberry may be considered as a type of the class of fruit syrups, the official process of manufacture being equally applicable to strawberries, blackberries, currants, cherries, etc. The object of setting the crushed fruit aside at a moderate temperature, 20° to 25° C. (68° to 77° F.), for several days, is to insure the complete destruction of certain undesirable principles known as pectin, or *vegetable jelly*, which, if allowed to

remain in the fruit juice, would cause the syrup to gelatinize and readily spoil.

The complete removal of pectin is shown by the test with alcohol, as the filtered juice should mix clear with half its volume of the latter, which will not occur as long as pectin is present; a concentrated solution of magnesium sulphate should also leave the filtered juice unaffected.

The fermentation of fruit juices is usually conducted in casks or containers tightly closed but provided with a suitable means of escape for the carbon dioxide gas generated during the process, as shown in Fig. 202; the end of the fermentative process is indicated when gas-bubbles cease to escape through the water contained in the small bottle. Experience has shown that the addition of a small quantity of sugar (2 per cent. of the weight of the fruit) hastens fermentation, preserves the color, and facilitates subsequent filtration of the juice.

Fig. 202.

After removal of the pectin, the pulp is expressed and the juice allowed to subside in well-closed vessels, in a cool place, for two or three days until clear; the supernatant liquid must be carefully decanted or withdrawn and passed through a previously-wetted paper filter. Sugar should be added to the filtrate without delay and dissolved by stirring before the mixture is heated to boiling; any albuminous matter remaining in the juice is coagulated by heating and removed by subsequent straining. The mixture of filtered juice and sugar must not be boiled for any length of time, but the heat should be withdrawn when the syrup begins to boil quietly after the first frothing and rising of the liquid.

7. *Syrupus Tolutanus.* The official formula directs that a strong alcoholic solution of balsam of tolu be mixed with sugar and precipitated calcium phosphate, the alcohol being subsequently evaporated spontaneously in a warm place; the residue is triturated with cold water and filtered through paper, and to the filtrate, heated to about 60° C. (140 F.), the remainder of the sugar is added and dissolved by agitation. The short contact of cold water with the finely-divided balsam of tolu will scarcely dissolve much of the odorous principles, and the heating to 60° C. appears more appro-

priate before than after filtration of the mixture, as in the latter case it simply facilitates solution of the sugar, which is equally well accomplished in the cold. If all the alcohol be allowed to remain, as in the case of syrup of orange, and the aqueous mixture be set aside, with frequent agitation, for six or eight hours, before filtration, a much finer flavored syrup will be obtained, since the presence of 5 per cent. of alcohol increases the solubility of the balsamic principles in the water. In case the alcohol is retained, the water and sugar ordered in the official formula must be reduced correspondingly, to 450 Cc. and 800 Gm., respectively.

8. *Syrupus Zingiberis.* According to the Pharmacopœia, syrup of ginger should be prepared from fluid extract of ginger, by mixing this with precipitated calcium phosphate, evaporating the alcohol, mixing the residue with water, filtering, and dissolving sugar in the filtrate. This does not yield a syrup of decided ginger odor or taste, for the reason that the cold water fails to take up sufficient of the oleo-resinous principles remaining with the calcium phosphate. A syrup of stronger aroma and pungency and better suited as a flavoring agent to disguise the unpleasant taste of saline and other medicines, may be obtained by the following modification of the official formula: Mix 20 Cc. of alcohol with 30 Cc. of fluid extract of ginger and incorporate 30 Gm. of precipitated calcium phosphate; gradually add 450 Cc. of water and set the mixture aside, with frequent agitation, for six or eight hours; then filter and wash the filter with water so as to obtain 500 Cc. of filtrate, in which dissolve 800 Gm. of sugar, by agitation without heat.

B. Medicated Syrups.

1. *Syrupus Acaciæ.* This syrup is prepared by mixing 1 volume of mucilage of acacia with 3 volumes of simple syrup, and is preferably made extemporaneously, owing to its tendency to deteriorate unless kept in a cold place; mucilage of acacia spoils more readily than a well-made syrup, and it is, therefore, of prime importance that the mucilage be fresh. Each Cc. of the syrup represents 0.378 Gm. of acacia.

2. *Syrupus Acidi Hydriodici.* Syrup of hydriodic acid is officially prepared by adding a freshly-made solution of hydriodic acid, containing potassium hypophosphite, to simple syrup; it contains 1 per cent. by weight of absolute hydriodic acid, equal to about 0.013 Gm. in each Cc. The syrup when freshly made is colorless, and keeps well for some time if preserved in completely filled bottles, in a dark place; gradually, iodine is liberated and the syrup becomes colored, and if more than pale straw-colored, it should be rejected. (For further remarks, see Iodine and its Compounds).

3. *Syrupus Allii.* Syrup of garlic owes its value to an essential oil, present in the fresh bulbs in larger proportion than in the dry, and readily extracted by maceration with diluted acetic acid, as

directed by the Pharmacopœia. The sugar must be dissolved without heat, and contact with metals must be avoided.

4. *Syrupus Althæa.* In the official process for this syrup the cut althæa is first washed with cold water to remove dust and foreign matter, and then macerated for one hour with cold water, to which about 8 per cent. of alcohol has been added as a preservative; the mixture is frequently stirred, and finally strained *without expression.* Cold water is preferable to warm water, as the latter produces a thick, ropy mucilage. After the sugar has been dissolved in the infusion, glycerin, to the amount of 10 per cent. by volume of the desired finished product, is added to preserve the rather unstable syrup. It must be preserved in completely filled bottles, in a cool place.

5. *Syrupus Calcii Lactophosphatis.* The first step in the preparation of this syrup is the solution of calcium carbonate in lactic acid diluted with water, producing calcium lactate; the addition of phosphoric acid causes the precipitation of calcium phosphate, which will be redissolved by the lactic acid and excess of phosphoric acid present, upon the further addition of water. If the phosphoric acid be diluted with about twice its volume of water, before it is added to the solution of calcium lactate, less trouble will be experienced, and, instead of forming a dense magma, the calcium phosphate will redissolve as fast as formed. The acid liquid, after the addition of water, is filtered, and to the filtrate, orange flower water and sugar are added, and the whole then shaken until dissolved. Each Cc. of the finished syrup represents 0.02584 Gm. of tri-calcium phosphate.

6. *Syrupus Calcis.* Advantage is taken, in the preparation of this syrup, of the well-known fact that sugar largely increases the solubility of lime in water, and this solubility varies with the proportion of sugar to the water used; according to Peligot, 100 parts of sugar contained in 250 parts of aqueous solution, will take up 26.5 parts of lime, while the same quantity of sugar in 2000 parts of solution takes up only 18 parts of lime. Choice lime should be used—as free from carbonate and other impurities as possible. The official syrup of lime is of uncertain strength, the Pharmacopœia not having fixed a definite proportion, but, when freshly made, it contains probably 0.032 Gm. of calcium oxide in every Cc. The direction to boil the lime, sugar, and water together for five minutes, is not essential, except to gain time, for cold maceration with frequent agitation will cause an equally large amount of lime to be dissolved; but longer time is necessary—possibly two or three days. Syrup of lime changes very rapidly upon exposure to air, and should, therefore, be kept in well-stoppered bottles.

7. *Syrupus Ferri Iodidi.* Syrup of ferrous iodide is made by adding a hot, freshly-prepared solution of iodide of iron to simple syrup. The official syrup contains about 10 per cent. by weight of ferrous iodide, or about 0.134 Gm. in each Cc.; it should be preserved in small, completely-filled bottles, in a place accessible to sunlight. On exposure to air, the color of the syrup slowly changes to yellow

and afterward to brown, the change of color proceeding from the exposed surface downward; when such a change is noticed, exposure of the syrup to direct sunlight will restore the original color. (For further remarks, see the Official Preparations of Iron.)

8. *Syrupus Ferri, Quininæ et Strychninæ Phosphatum.* The preparation of this syrup presents no difficulties if the official directions be followed. An aqueous solution of soluble phosphate of iron is mixed with phosphoric acid, and in this acid liquid the alkaloids, quinine and strychnine, are dissolved; the solution is filtered into glycerin and then mixed with simple syrup. Each Cc. of the syrup contains 0.030 Gm. of quinine, 0.020 Gm. of soluble phosphate of iron, and 0.002 Gm. of strychnine; the presence of 10 per cent. of glycerin favors the stability of the syrup, but a gradual darkening of the color cannot be avoided, although it may be retarded by keeping the syrup in completely-filled bottles, in a dark place.

9. *Syrupus Hypophosphitum.* By this name the Pharmacopœia recognizes a syrup of the hypophosphites of calcium, potassium, and sodium flavored with spirit of lemon; it is prepared by making a solution of the three salts in water, acidulating the same with hypophosphorous acid, and in it dissolving the sugar by agitation. Each Cc. of the syrup contains 0.045 Gm. of calcium hypophosphite, 0.015 Gm. each of potassium and sodium hypophosphites, and 0.002 Gm. of dilute hypophosphorous acid.

10. *Syrupus Hypophosphitum cum Ferro.* This syrup is made by dissolving 10 Gm. each of ferrous lactate and potassium citrate in 1000 Cc. of the preceding syrup; it darkens considerably by age, and should therefore be freshly made when wanted. Ferrous lactate in the form of crystalline crusts is the best of the commercial varieties, and should alone be used in the preparation of this syrup.

11. *Syrupus Ipecacuanhæ.* Syrup of ipecac is made from the fluid extract of the drug, which is well shaken with a mixture of acetic acid and water, for the purpose of bringing the active principle (emetine) into aqueous solution and of rejecting those undesirable constituents which are apt to cause flocculi in the syrup; after filtration, glycerin is added to the clear liquid, and then the sugar, after which the mixture is well shaken, until dissolved. Formerly, syrup of ipecac was likely to sour in warm weather, but this difficulty is now obviated by the presence of 10 per cent. of glycerin; each Cc. represents 0.070 Gm. of ipecac.

12. *Syrupus Krameriæ.* This syrup is prepared by mixing fluid extract of krameria with simple syrup, in the proportion of 45 volumes of the former to 55 volumes of the latter; each Cc. represents 0.45 Gm. of krameria.

13. *Syrupus Lactucarii.* In the official process for this syrup, tincture of lactucarium is slowly incorporated with sugar and precipitated calcium phosphate, after which water is added in small portions at a time; the mixture is then filtered, and in the filtrate sugar is dissolved without heat. The object of this treatment is to

obtain a clear, transparent syrup, which can be attained if the tincture has been properly prepared and freed from the caoutchouc-like constituent present in the drug. Each Cc. of the syrup represents the active virtues of 0.050 Gm. of lactucarium.

14. *Syrupus Picis Liquidæ.* Tar always contains certain impurities which are readily soluble in cold water, and these it is intended to remove in the process officially directed for the syrup. Sand is mixed with the tar, before the addition of cold water, in order to facilitate the washing, which is continued for twelve hours with frequent stirring. After decanting and rejecting the first liquid, boiling distilled water is added to the purified tar, and the mixture is well stirred during fifteen minutes, after which glycerin is added and maceration continued for twenty-four hours, during which time the soluble constituents of the tar are extracted; sugar is dissolved in the clear liquid, which has been decanted and filtered, with the aid of a gentle heat. Each Cc. represents the virtues of 0.075 Gm. of tar.

15. *Syrupus Pruni Virginianæ.* Wild cherry is macerated for twenty-four hours with a mixture of one volume of glycerin and two volumes of water, during which time a peculiar reaction or fermentation goes on between certain constituents of the bark, resulting in the formation of hydrocyanic acid, and a volatile oil identical with oil of bitter almond. After maceration the drug is slowly percolated to practical exhaustion, and in the percolate the sugar is dissolved without heat. Enough menstruum should be added to the powdered drug to thoroughly moisten it, and the percolator kept tightly closed to prevent loss of the hydrocyanic acid; a No. 20 powder being rather coarse, the mixture must be very firmly packed, so that the drug may be slowly exhausted. The presence of 15 per cent. by volume of glycerin will prevent the fermentative changes frequently observed heretofore in the finished syrup, although at the same time it increases the extraction of tannin from the bark. The amount of hydrocyanic acid present in the syrup is a very uncertain quantity, nor does it remain constant, owing to exposure and its volatile and unstable character.

16. *Syrupus Rhei.* The official formula directs a solution of potassium carbonate to be added to fluid extract of rhubarb, prior to its admixture with simple syrup; a small quantity of spirit of cinnamon is also added as a flavoring agent. The addition of an alkali prevents the separation of resinous matter, by retaining the same in solution, and thus a clear syrup is obtained. The use of water for solution of the potassium carbonate and the addition of 5 per cent. of glycerin appear quite unnecessary, since the alkali can be dissolved in a part of the simple syrup, and syrup of rhubarb thus prepared keeps admirably well. Each Cc. represents 0.100 Gm. of rhubarb.

17. *Syrupus Rhei Aromaticus.* Aromatic or spiced syrup of rhubarb is made, according to the Pharmacopœia, by mixing 15 volumes of the aromatic tincture of rhubarb with 85 volumes of

simple syrup; the result is a cloudy syrup, owing to the suspension of partially precipitated resinous matter. If a perfectly clear syrup is desired, it may be obtained by adding a small proportion of borax, about ½ per cent., or 5 Gm. for every 1000 Cc. of finished syrup; the borax should be dissolved in the tincture, before the addition of the syrup.

18. *Syrupus Rosæ.* This preparation is a simple mixture of 1 volume of fluid extract of rose with 7 volumes of syrup. It has a beautiful red color and an agreeably astringent taste, and, although reckoned among the medicated syrups, is more frequently employed as a flavoring agent for saline and other mixtures.

19. *Syrupus Rubi.* The official syrup of blackberry is made by mixing 1 volume of fluid extract of blackberry bark with 3 volumes of syrup. It has a strongly astringent taste and is of a deep reddish-brown color.

20. *Syrupus Sarsaparillæ Compositus.* In the preparation of this syrup a mixture is first prepared of the fluid extracts of sarsaparilla, senna, and liquorice root, and a very small quantity of the oils of sassafras, anise, and gaultheria; this mixture, after the addition of water, is well shaken and set aside for an hour to allow separation of inert, insoluble matter, after which it is filtered. Sugar is dissolved in the filtrate, with the aid of only a gentle heat, to avoid loss of the volatile oils. The finished syrup contains very nearly 8 per cent. of alcohol derived from the fluid extracts, and therefore a less quantity of sugar than most other syrups. The present official formula differs from those formerly employed, in omitting guaiacum wood and pale rose petals. Each Cc. of the finished syrup represents 0.200 Gm. of sarsaparilla, 0.015 Gm. each of senna and liquorice root, and a trace each of the oils of gaultheria, anise, and sassafras.

21. *Syrupus Scillæ.* Syrup of squill is prepared by dissolving sugar in vinegar of squill; the latter contains considerable albuminous matter, which it is intended to remove by the official directions to boil and filter the liquid before the addition of the sugar. On account of the very acid character of the preparation, contact with metallic vessels should be avoided. Each Cc. represents the active virtues of 0.045 Gm. of squill.

22. *Syrupus Scillæ Compositus.* Compound syrup of squill, also sold under the name of *hive syrup*, is made from the fluid extracts of squill and senega, as follows: The two fluid extracts are mixed, evaporated on a water-bath to about half their bulk, and then mixed with water; when cold, the liquid is intimately mixed with precipitated calcium phosphate and filtered, to remove pectin compounds and albuminous matter, which are otherwise likely to pass through the filter. If necessary, the liquid should be returned to the filter until it passes through *perfectly clear*. To the clear filtrate is added a definite quantity of tartar emetic, previously dissolved in hot water, and then the prescribed quantity of sugar, which is dissolved without heat. Each Cc. of the syrup contains 0.002 Gm. of

antimony and potassium tartrate and the active principles of 0.080 Gm. each of squill and senega.

23. *Syrupus Senegæ.* Syrup of senega is made by dissolving sugar in fluid extract of senega previously diluted with water. Senega is rich in pectin compounds, the separation of which, in liquid preparations of the drug, is avoided by the presence of alkalies. Fluid extract of senega contains 5 per cent. of ammonia water, and the Pharmacopœia recommends a further addition of 2½ per cent., before diluting the fluid extract with water. The mixture is filtered after standing three or four hours, and in the *clear* filtrate the sugar is dissolved without heat. Each Cc. of the syrup represents 0.200 Gm. of senega.

There appears to be no objection to preparing the syrup as wanted, by mixing one volume of fluid extract of senega with four volumes of simple syrup, this mixture keeping equally as well as the former more tedious preparation.

24. *Syrupus Sennæ.* The official process for making syrup of senna consists in preparing a strong infusion of the leaves, mixing this with alcohol and oil of coriander, removing the precipitate by filtration, and in the filtrate dissolving the sugar without heat; each Cc. represents the virtues of 0.250 Gm. of senna.

Long-continued digestion of senna leaves at 60° C. (140° F.), as directed in the Pharmacopœia, is of no advantage, as the cathartic principles can be extracted in less time, and long maceration brings an undesirable amount of gum into solution; digestion for six or eight hours is no doubt sufficient when followed by expression and a further treatment of the dregs on the strainer by percolation with hot water. Solution of the sugar in the clear liquid is greatly facilitated by placing a well-corked bottle, containing both, in a moderately warm water-bath and agitating frequently. The gummy matter is precipitated upon the addition of alcohol, and some time must be allowed for complete separation of the precipitate, otherwise subsequent filtration of the liquid will be difficult; the clear liquid is decanted and the remainder filtered, the filter being washed with water.

CHAPTER XVII.

MUCILAGES, HONEYS, AND GLYCERITES.

Mucilages.

THE preparations recognized in the Pharmacopœia under this name are viscid adhesive liquids formed by solution of mucilaginous principles in water; with one exception they are unstable and readily undergo putrefactive changes in warm weather, hence they should be freshly prepared when wanted. The four official mucilages are those of acacia, sassafras pith, tragacanth, and elm.

Mucilago Acaciæ. The Pharmacopœia recommends that acacia be washed with cold water before it is brought into solution, for the purpose of removing foreign matter often adhering to the outer surface. The official formula will produce quite a viscid liquid containing 34 per cent. of acacia, each Cc. representing 0.378 Gm. Owing to the fact that the solution of acacia becomes denser as it progresses, stirring or agitation of the mixture will be found somewhat difficult toward the end of the process, and solution can be more readily effected by what is known as circulatory displacement (see page 114), that is, the suspension of the washed acacia in the water, in a bag of loosely textured cloth, to be occasionally moved about in the liquid so that fresh portions of the water may continually displace the solution formed, and thus complete solution be more rapidly effected. Pieces of clear, white acacia should be selected for the mucilage, which, when made, should be preserved in completely filled bottles, *in a cool place.*

Mucilago Sassafras Medullæ. Mucilage of sassafras pith is made by macerating the pith in cold water for three hours and then straining; the mixture should be kept in a covered vessel and occasionally stirred with a glass rod. Each Cc. represents 0.02 Gm. of sassafras pith.

Mucilago Tragacanthæ. The official directions for preparing mucilage of tragacanth are, to add the tragacanth to a boiling mixture of glycerin and water and then macerate for twenty-four hours, with frequent stirring; after the addition of more water, the mass is beaten to a uniform consistence and then forcibly expressed through muslin. Mucilage of tragacanth forms a somewhat opaque semi-liquid jelly containing 6 per cent. of tragacanth; the presence of 18 per cent. of glycerin prevents decomposition. Tragacanth is only partially soluble in water, but absorbs the latter and swells to a gelatinoid mass.

Mucilago Ulmi. Mucilage of elm, although still recognized in

the Pharmacopœia, is but very rarely prepared by pharmacists; the official directions are to add 6 Gm. of bruised elm to 100 Cc. of water and digest for one hour, in a covered vessel, on a water-bath. Mucilage of elm, like that of sassafras pith, spoils very readily, and should be freshly made when wanted.

Honeys.

Clarified honey, or Mel Despumatum of the Pharmacopœia, is prepared by mixing honey with 2 per cent. of its weight of paper-pulp and heating the mixture on a water-bath as long as any scum rises to the surface; the scum is carefully removed with a skimmer and sufficient distilled water added to restore loss by evaporation, after which the mixture is strained and 5 per cent. of its weight of glycerin is added to the strained liquid, for the purpose of better preservation.

Medicated honeys are simply mixtures of clarified honey with certain medicinal agents, and are, as a rule, prepared extemporaneously.

Only one medicated honey is recognized in the Pharmacopœia, namely, Mel Rosæ, or honey of rose, which is made by mixing fluid extract of rose with clarified honey, in such proportion that the finished product shall contain the astringent virtues of 12 Gm. of rose petals in every 100 Gm.; this is about equal to a mixture of 12 Cc. of fluid extract of rose with 64 Cc. of clarified honey.

Glycerites.

This valuable class of preparations consists of solutions of the medicinal agents in glycerin; they are permanent and are readily miscible with water or alcohol. Of the official glycerites, five are liquid and one solid.

Glyceritum Acidi Carbolici. This glycerite is conveniently prepared by placing crystallized carbolic acid and glycerin together in a porcelain dish and warming the mixture on a water-bath until perfect solution is effected; each Gm. of the finished glycerite represents 0.20 Gm. of carbolic acid, which is equal to about 110 grains in one fluidounce.

Glyceritum Acidi Tannici. Although tannin is perfectly soluble in cold glycerin, the solution of so large a proportion as directed in the official glycerite is best effected by the aid of heat; contact with metallic vessels must be carefully avoided, and the tannin and glycerin should be intimately mixed with a glass rod before heat is applied. When solution is completed, a deep green, transparent liquid results, which should be strained, while still warm, through flannel or a pledget of cotton. Glycerite of tannin contains 20 per cent. of tannin, or about 0.300 Gm. in each Cc., which is equal to about 120 grains in one fluidounce.

Glyceritum Amyli. The official directions for preparing glycerite of starch are to stir 10 parts of starch with 10 parts of water and

80 parts of glycerin, to a homogeneous mixture, and then apply a gradually increased heat until a translucent jelly is formed. As starch usually occurs in lumps, it is necessary to first rub it, in a mortar, into a fine powder, which should be transferred to a porcelain capsule, and then mixed with the water and glycerin, so as to avoid loss, which is unavoidable if the mixture be made in the mortar; heat must be applied cautiously and the mixture *constantly* stirred with a thick glass rod or a wooden spatula, to avoid scorching and consequent discoloration. The liquid gradually thickens as the heat is increased, and the entire disappearance of white spots indicates perfect solution. The high heat indicated in the official formula is necessary to effect the rupture of the starch granules, without which solution of the starch cannot take place; to insure uniform heating, wire gauze should invariably be interposed between the capsule and the flame. Glycerite of starch is hygroscopic, therefore it must be preserved in tightly closed jars, so as to avoid contact with air.

Glyceritum Boroglycerini. The preparation of this glycerite involves first the production of boroglycerin, known also as boroglyceride or glyceryl borate, and secondly, the solution of this compound in glycerin. When boric acid and glycerin are heated together to about 150° C. (302° F.), chemical action sets in, water being given off, while a new compound, glyceryl borate, is formed, which upon cooling is obtained as a transparent, almost colorless and very hygroscopic mass; the mixture must be frequently stirred to break up the constantly forming film, and care must be observed that the heat prescribed be neither exceeded nor continued longer than necessary, so as to avoid a yellowish or brownish coloration. Thirty-one parts of boric acid and 46 parts of glycerin will unite to form 50 parts of glyceryl borate; hence in the official process the reaction is known to be complete when the weight of the mixture has been reduced to 500 Gm.; then, while still hot, an equal weight of glycerin is added and thoroughly incorporated, thus making a 50 per cent. solution of boroglycerin. Each Cc. contains about 0.683 Gm. of boroglycerin, which is equal to about 312 grains in a fluidounce.

Glyceritum Hydrastis. In the official process for glycerite of hydrastis, the finely powdered root is exhausted with alcohol by percolation, the resulting tincture mixed with water and the alcohol removed by distillation, in order to precipitate the resinous matter; after dilution of the residue with more water, the mixture is set aside for twenty-four hours and then filtered, the filter being washed with water. To the filtrate, an equal volume of glycerin is added and the whole thoroughly mixed. Each Cc. of the finished glycerite represents 0.500 Gm. of hydrastis, or a fluidounce contains about 228 grains.

According to Prof. Lloyd, the best results will be obtained if the official directions be modified to the extent that the alcoholic tincture, without the addition of water, be concentrated to a syrupy consistence

by distillation or otherwise, and then poured into *ice-cold* water equal in quantity to one-half the weight of drug used; the soft, oily, resinous matter separates readily and can be removed by filtration after a few hours' rest. The filtrate must be brought to a volume of 500 Cc. for every 1000 Gm. of drug operated upon, by washing the filter with cold water, after which the glycerin is added and the mixture shaken thoroughly.

This glycerite is chiefly intended to furnish a fluid preparation of hydrastis which shall be miscible with water in all proportions without precipitation.

Glyceritum Vitelli. Glycerite of yelk of egg, or glyconin, is a mixture of 45 parts of yelk of egg and 55 parts of glycerin, of about the consistence of honey, which will keep for a long time if preserved in well-stoppered bottles, so as to prevent the absorption of moisture from the air. In order to obtain a satisfactory preparation, the yelk of egg should be carefully separated from the albumen, and the membrane enclosing the yelk then ruptured, so that only the pure yelk may be weighed; the glycerin should be added gradually, with constant trituration.

CHAPTER XVIII.

ELIXIRS.

THE word "elixir" is said to be of an ancient origin, and derived, according to Dr. Charles Rice, from two Arabic words, pronounced *al-iksir;* the Arabic *iksir* comes from the Greek word ξήριον, meaning a dry powder, such as was used for dusting wounds. For a long time the word was applied by alchemists to the wonderful transformation powder used in the supposed conversion of base metals into silver and gold. Later on, the term was also applied to liquids, and used to designate certain compound tinctures, for which rare medicinal properties were claimed. In this latter sense the term elixir is still used to some extent in Continental Europe, and, as a rule, such preparations are characterized by an unpleasant taste. In modern American pharmacy the word has come to mean an entirely different class of preparations, the distinguishing features of which are a pleasantly aromatic sweet taste, and the presence of alcohol varying in proportion from 20 to 25 per cent. by volume. Prior to 1865, only two elixirs of this kind were used to any extent in this country—namely, *Elixir of calisaya* and *Elixir of ammonium valerianate;* but through the efforts of enterprising manufacturers the list was rapidly augmented and reached its height between 1870 and 1875. A reaction, however, gradually set in, and at the present day many once-popular elixirs have fallen into disuse. There can be no doubt that a sweet, aromatic, and slightly alcoholic liquid forms a pleasant vehicle for many remedies, but the presence of 25 per cent. of alcohol may, in some instances, be positively injurious, and, moreover, the active ingredients are frequently present in such small quantities as to render the medicinal value of the preparation doubtful.

The American Pharmaceutical Association, in order to secure uniformity in the composition of the many elixirs dispensed by pharmacists, has published a series of 86 formulas for elixirs, in the *National Formulary.* This book was issued in 1888, and a revised edition is shortly to appear. Another series, containing about 275 formulas for elixirs and many valuable directions in manipulation, was published by J. U. Lloyd in 1892, under the title *Elixirs and Flavoring Extracts.* Many elixirs can be prepared extemporaneously by simple solution of the medicinal ingredient in the desired vehicle; as, for instance, the elixirs of the alkali bromides, citrates, salicylates, and hypophosphites, elixir of pyrophosphate of iron, elixir of gentian, both simple and ferrated, etc.

It is often desirable to impart color to an elixir, but since not all

coloring agents are equally well suited for acid and alkaline liquids, it becomes necessary to exercise proper discretion. For acid or neutral liquids the *National Formulary* recommends either the simple or compound tincture of cudbear, the former for a bright-red and the latter for a brownish-red tint; of either tincture, two fluidrachms will suffice to color a pint of elixir. For alkaline liquids, such as elixir of ammonium valerianate, the coloring agent should be a solution of carmine, which is best prepared with the aid of ammonia water; the *National Formulary* furnishes a satisfactory formula for the same.

The Pharmacœpia recognizes only two elixirs—namely, aromatic elixir and elixir of phosphorus; the former is simply a convenient vehicle or base for the preparation of many other elixirs, and has the following volume percentage composition: volatile oils, 0.33 per cent.; deodorized alcohol, 24.67 per cent.; syrup and distilled water, each 37.5 per cent. On account of the turbidity caused by the solution of the oils when mixed with the aqueous liquid, the addition of precipitated calcium phosphate becomes necessary; if the mixture be then well shaken, a clear filtrate can at once be obtained.

Elixir of phosphorus contains 0.00025 Gm. of phosphorus in each Cc., and also 55 per cent. by volume of glycerin; since phosphorus is very readily oxidized, the elixir should not be made in large quantities, and should be preserved in well-filled, tightly-stoppered, dark bottles. By following the pharmacopœial directions exactly, a clear solution can readily be made.

COMPOSITION OF OFFICIAL ELIXIRS.

Name.	Composition.	
Elixir Aromaticum	Compound Spirit of Orange	12 Cc.
	Deodorized Alcohol	238 "
	Syrup	375 "
	Distilled Water	375 "
Elixir Phosphori	Spirit of Phosphorus	210 Cc.
	Oil of Anise	2 "
	Glycerin	550 "
	Aromatic Elixir	238 "

It is not within the scope of this work to furnish numerous formulas for elixirs, but there are two elixirs which are deserving of special consideration, because they have been the source of much vexation to pharmacists; these are the elixir of the phosphates of iron, quinine, and strychnine, and the elixir of pepsin, bismuth, and strychnine.

Elixir Ferri, Quininæ et Strychninæ Phosphatum. While this preparation was originally intended to be an elixir of the three phosphates, very few manufacturers make this claim for their preparation, and the published formulas simply direct the use of phosphate of iron with the pure alkaloids, or the sulphates or hydrochlorides, of quinine and strychnine. Some of the commercial elixirs of the above name form clear mixtures with water; hence numerous efforts have been made to prepare an elixir which shall be permanent at all temperatures,

and miscible with water *in all proportions.* Want of uniformity in strength is another unfortunate feature in the many elixirs of phosphate of iron, quinine, and strychnine dispensed by pharmacists; some contain twice as much iron and quinine as others, and the amount of strychnine varies still more.

As a rule, the elixirs of phosphate of iron, quinine, and strychnine prescribed by physicians and offered for sale by manufacturers are supposed to be of one-half the strength of Easton's syrup, and to contain in each fluidrachm 1 grain of phosphate of iron, $\frac{1}{2}$ grain of phosphate of quinine and $\frac{1}{64}$ grain of phosphate of strychnine. This strength has also recently (1894) been adopted by the American Pharmaceutical Association, although the formula of the new *National Formulary* (revised edition) will direct the quinine and strychnine to be held in solution as alkaloids, and not as phosphates. Some of the elixirs of phosphate of iron, quinine, and strychnine, made with pure alkaloids, form turbid mixtures with small quantities of water (1 or 2 volumes), but become perfectly clear if more water be added (8 volumes); this is particularly the case with those containing an additional amount of simple syrup or some glycerin. Of the various formulas in use for this class, the following furnishes a very satisfactory light-colored (yellowish-green) preparation:

Take of

Soluble Phosphate of Iron (U.S.P.)	128	grains.
Quinine, alkaloid	64	"
Strychnine, alkaloid	2	"
Alcohol	2	fluidounces.
Simple Syrup	2	"
Distilled Water	2	"
Aromatic Elixir, sufficient to make	16	"

Dissolve the alkaloids in the alcohol, add the syrup, and then 8 fluidounces of aromatic elixir. Dissolve the iron salt in the distilled water, by aid of a gentle heat (neutralizing the solution with ammonia, if necessary), mix with the alkaloidal solution, and add sufficient aromatic elixir to bring the total volume up to 16 fluidounces.

If an elixir is desired containing the quinine and strychnine as phosphates, in perfect solution with the phosphate of iron, and yet not unpleasantly acid (for a large excess of phosphoric acid will accomplish the purpose), some other substance must be added which shall prevent precipitation. After numerous experiments I have found ammonium acetate to produce the best results and to yield an elixir which, even if made of double the stated strength, remains clear at a freezing temperature and mixes clear with water in all proportions. The very small proportion of ammonium acetate required is not in any way hurtful, and need not be considered any more than the alkali citrate in the soluble phosphate of iron.

All elixirs containing soluble phosphate of iron will darken materially if exposed to light, and particularly that made by the following formula: hence they should be preserved and dispensed in amber-colored bottles.

Take of

Soluble Phosphate of Iron (U.S.P.)	128 grains.
Quinine, alkaloid	64 "
Strychnine, alkaloid	2 "
Phosphoric acid, 85 per cent	15 minims.
Acetic Acid, 36 per cent.	225 grains.
Ammonium Carbonate	71 "
Alcohol	1 fluidounce.
Distilled Water } of each a sufficient quantity to make	16 fluidounces.
Aromatic Elixir } of each a sufficient quantity to make	16 fluidounces.

Dissolve the quinine and strychnine in the alcohol, add 6 fluidounces of aromatic elixir, and then the phosphoric acid. Add the ammonium carbonate to the acetic acid contained in a beaker or graduate, and when the solution is complete, add enough distilled water to bring the volume up to 6 fluidrachms. Mix the ammonium acetate solution with the solution of quinine and strychnine phosphates, and add enough aromatic elixir to make the liquid measure 14 fluidounces. Dissolve the iron scale salt in $\frac{1}{2}$ fluidounce of distilled water by the aid of a gentle heat, and if the solution be acid to test-paper, neutralize exactly with ammonia water, and add enough aromatic elixir to bring the volume up to 2 fluidounces. Finally mix the two solutions.

This preparation conforms in strength to that claimed for the majority of the elixirs offered on the market, containing, in each fluidrachm, 1 grain of phosphate of iron, and $\frac{1}{2}$ grain of quinine and $\frac{1}{64}$ grain of strychnine, both in combination with phosphoric acid. If an elixir of twice the strength be desired, it can be readily obtained by doubling all the ingredients except the aromatic elixir.

With some samples of soluble phosphate of iron, a slightly increased quantity of the ammonium acetate solution may be necessary, possibly owing to a loss of water and consequent relative increase of the proportion of the iron salt.

Elixir Pepsini, Bismuthi et Strychninæ. One of the chief difficulties in connection with this elixir has been the preparation of a neutral liquid which shall permanently retain all three of the active ingredients in solution. Pepsin is active only in acid fluids, and its action is inhibited, and in the course of time destroyed, by alkalies. The official bismuth and ammonium citrate is not a very stable compound, and although perfectly soluble when freshly prepared, in plain water, it loses this property in time, owing to decomposition of the ammonium citrate; in alkaline liquids it retains its solubility, but an alkaline fluid will not only interfere with the pepsin, but may also throw the strychnine out of solution. The best that has been accomplished thus far has been a neutral solution of these three active ingredients—of doubtful stability, however, and likely to lose the bismuth salt by precipitation.

Since physicians desire and extensively prescribe the elixir of pepsin, bismuth, and strychnine, it becomes the duty of the pharmacist to so prepare it that a permanent solution shall result; this can only be done with a liquid of acid reaction. In 1888, the

late R. Rother called attention to a permanent solution of bismuth and sodium tartrate of acid reaction, and suggested its use in place of the bismuth and ammonium citrate. I would recommend the following formula, which I have found to yield an unexceptionable preparation:

Take of

Pepsin in scales (U.S.P. standard)	64 grains.
Strychnine	2 "
Tartaric Acid	2 "
Distilled Water	4 fluidounces.
Glycerin	2 "
Glycerite of Bismuth and Sodium Tartrate	2 "
Caramel	4 drops.
Aromatic Elixir	8 fluidounces.

1. Dissolve the pepsin in a mixture of 1 fluidounce each of glycerin and water. 2. Dissolve the strychnine with the tartaric acid in 2½ fluidounces of water, and add the balance of the glycerin, the bismuth solution, the caramel, and the aromatic elixir. 3. Finally, pour the pepsin solution into the other liquid. In place of the pepsin a corresponding quantity of glycerite of pepsin, *free from mineral acid*, may be used, and in that case the water and glycerin must be reduced accordingly.

This preparation contains ½ grain of official pure pepsin, 2 grains of bismuth and sodium tartrate, and $\frac{1}{64}$ grain of strychnine, in each fluidrachm.

The glycerite of bismuth and sodium tartrate referred to in the above formula can be prepared as follows:

Take of

Bismuth Subnitrate	1142 grains.
Nitric Acid	19 fluidrachms
Tartaric Acid	1720 grains.
Sodium bicarbonate	1954 "
Glycerin	8 fluidounces.
Distilled Water	a sufficient quantity.

Dissolve the bismuth salt in the nitric acid previously diluted with 10 fluidrachms of water; to the solution, slowly add 16 fluidounces of water. Now add 860 grains of powdered tartaric acid, and then, gradually, 977 grains of sodium bicarbonate. Dilute the magma of bismuth tartrate with 32 fluidounces of water. Set the mixture aside for five or six hours and wash by decantation and repeated affusion of water, until all nitric acid has been removed; drain the precipitate on a paper filter. Mix 977 grains of sodium bicarbonate with 5 fluidounces of water and gradually add 860 grains of powdered tartaric acid, warming slightly to obtain a perfect solution. Transfer the precipitate of bismuth tartrate to the solution of sodium tartrate and stir until dissolved; filter the solution, add the glycerin, and evaporate it on a water-bath, or dilute it with water, as may be necessary, so that the liquid shall measure 16 fluidounces. Each fluidrachm of this solution contains 16 grains of bismuth and sodium tartrate with an excess of sodium tartrate.

CHAPTER XIX.

SPIRITS OR ESSENCES.

In the Pharmacopœia, the term "spiritus" is used to designate an alcoholic solution of volatile substances, chiefly volatile oils; in a few cases, water also is added. Of the twenty-five spirits recognized in the Pharmacopœia, all but five can be conveniently prepared by the pharmacist, as they are quickly made and require only the ordinary apparatus usually found in the store; as a rule, they are prepared by simple solution of the liquid or gaseous body in alcohol, although sometimes distillation is resorted to. Whenever volatile oils are used in the preparation of spirits, only the very best should be selected, as the value of the finished product depends entirely upon the quality of the oil; particular attention should be paid to those oils likely to have assumed a terebinthinate odor, such as the oils of juniper, lemon, nutmeg, and orange peel.

The following is a list of the official spirits, together with their composition:

Official name.	Composition.
Spiritus Ætheris	Ether 1 volume, Alcohol 3 volumes.
Spiritus Ætheris Compositus (Hoffman's Anodyne).	Ethereal Oil 1 volume, Ether 13 volumes Alcohol 26 volumes
Spiritus Ætheris Nitrosi	An alcoholic solution of Ethyl Nitrite, containing, when freshly made, between 4 and 5 per cent. of the ethereal liquid.
Spiritus Ammoniæ	An alcoholic solution of Ammonia containing 10 per cent. by weight of the gas.
Spiritus Ammoniæ Aromaticus	A hydro-alcoholic solution of normal Ammonium Carbonate, containing 70 per cent. by volume of Alcohol, 1 per cent. of Oil of Lemon, and $\frac{1}{8}$ per cent. each of Oil of Nutmeg and Oil of Lavender Flowers
Spiritus Amygdalæ Amaræ (Essence of Bitter Almond).	Oil of Bitter Almond 1 volume, Alcohol 80 volumes, and Distilled Water sufficient to make 100 volumes
Spiritus Anisi	Oil of Anise 1 volume, Deodorized Alcohol 9 volumes.
Spiritus Aurantii	Oil of Orange Peel 1 volume, Deodorized Alcohol 19 volumes
Spiritus Aurantii Compositus	Oil of Orange Peel 20 volumes, Oil of Lemon 5 volumes, Oil of Coriander 2 volumes, Oil of Anise $\frac{1}{2}$ volume, Deodorized Alcohol 72½ volumes.
Spiritus Camphoræ	Camphor 10 Gm., Alcohol sufficient to make 100 Cc. of solution.
Spiritus Chloroformi	Chloroform 6 volumes, Alcohol 94 volumes.
Spiritus Cinnamomi	Oil of Cinnamon 1 volume, Alcohol 9 volumes.

Spiritus Frumenti (Whiskey) .	An alcoholic liquid obtained by the distillation of the mash of fermented grain (usually of mixtures of corn, wheat, and rye), and at least two years old.
Spiritus Gaultheriæ	Oil of Gaultheria 1 volume, Alcohol 19 volumes
Spiritus Glonoini (Spirit of Nitroglycerin).	An alcoholic solution of Glonoin, or Nitroglycerin, containing 1 per cent. by weight of the substance.
Spiritus Juniperi	Oil of Juniper 1 volume, Alcohol 19 volumes.
Spiritus Juniperi Compositus .	Oil of Juniper 8 volumes, Oil of Caraway and Oil of Fennel each 1 volume, Alcohol 1400 volumes, Water sufficient to make 2000 vols.
Spiritus Lavandulæ	Oil of Lavender Flowers 1 volume, Deodorized Alcohol 19 volumes
Spiritus Limonis (Essence of Lemon).	A 5 per cent. alcoholic solution of Oil of Lemon; this spirit also contains in each liter the oil and coloring matter from 50 Gm of freshly grated lemon peel.
Spiritus Menthæ Piperitæ (Essence of Peppermint).	Oil of Peppermint 1 volume, Alcohol 9 vols; this spirit is colored green by peppermint herb.
Spiritus Menthæ Viridis (Essence of Spearmint).	Oil of Spearmint 1 volume, Alcohol 9 volumes; this spirit is colored green by spearmint herb
Spiritus Myrciæ (Bay Rum) . .	Oil of Myrcia 16 volumes, Oil of Orange Peel 1 volume, Oil of Pimenta 1 volume Alcohol 1220 volumes, Water sufficient to make 2000 volumes.
Spiritus Myristicæ (Essence of Nutmeg).	Oil of Nutmeg 1 volume, Alcohol 19 volumes.
Spiritus Phosphori (Tincture of Phosphorus).	A solution of Phosphorus in Absolute Alcohol representing 0.0012 Gm. in each Cc.
Spiritus Vini Gallici (Brandy) .	An alcoholic liquid obtained by the distillation of the fermented unmodified juice of fresh grapes, and at least 4 years old.

Special Remarks on Some Official Spirits.

Spiritus Ætheris Compositus. Commercial Hoffmann's anodyne varies greatly in composition, and is probably never identical with the official spirit—in fact, manufacturers do not claim this to be the case; hence the necessity for discrimination between the two preparations when physicians prescribe compound spirit of ether. The commercial varieties of Hoffmann's anodyne are often obtained as by-products in the rectification of ether, and consist of mixtures of heavy and light oil of wine, ether, alcohol, and water, brought up to a certain arbitrary standard, varying with different manufacturers.

Spirit Ætheris Nitrosi. This preparation is a very unstable solution, at least as far as the proportion of active ingredients is concerned; even under the most favorable conditions it deteriorates; to retard this change, as far as possible, the spirit should be preserved in small, well-stoppered bottles, in a cool, dark place. Spirit of nitrous ether should be purchased in original packages, and never in bulk drawn from carboys.

The chemical reactions involved in the manufacture of this spirit will be explained elsewhere, as also the official method of determining its quality.

Spiritus Ammoniæ. The object of directing the use of alcohol recently distilled and preserved in glass, is to avoid discoloration of the liquid, which is apt to occur if ammonia gas be dissolved in alcohol kept in barrels and containing organic impurities. Spirit of ammonia is of the same strength as official ammonia water, and is intended to be used in cases where the aqueous solution is inadmissible.

Spiritus Ammoniæ Aromaticus. Ammonia water is used in connection with official ammonium carbonate, for the purpose of converting the latter into the normal salt, as this alone is soluble in the alcoholic liquid; in order to complete the change, it is advisable to let the aqueous solution stand for twelve or twenty-four hours, before adding it to the mixture of oils and alcohol. Aromatic spirit of ammonia is of faint color when freshly prepared, but gradually becomes darker.

Spiritus Frumenti. Whiskey, as recognized by the Pharmacopœia, should contain from 50 to 58 per cent. by volume of alcohol, which is readily ascertained by aid of the alcoholometer described on page 57. 100 Cc. of whiskey, when evaporated to dryness, should not yield more than 0.25 Gm. of residue.

Spiritus Phosphori. The weighing of phosphorus requires considerable care, owing to its very inflammable nature; it should always be performed in water, and the phosphorus rapidly dried by means of filter-paper, before it is introduced into the absolute alcohol. The use of an upright condenser is necessary when heat is employed, to avoid ignition and loss of alcohol, which would occur in an unstoppered flask; agitation with cold absolute alcohol will also dissolve phosphorus, but it is a tedious process. Phosphorus is far more soluble in fixed oils or chloroform, but since spirit of phosphorus is used chiefly in the preparation of elixir of phosphorus, such solutions would be inadmissible. Phosphorus is rapidly oxidized upon exposure to air, and particularly when in solution, hence the spirit must be preserved in small, securely stoppered vials, in a cool, dark place.

Spiritus Vini Gallici. Official brandy should be at least four years old, and contain from 46 to 55 per cent. by volume of alcohol; the older the brandy the finer is its quality. 100 Cc. of brandy, upon evaporation to dryness, should not yield more than 1.5 Gm. of residue.

CHAPTER XX.

TINCTURES.

TINCTURE is the name applied to solutions of non-volatile or only partially volatile substances, in liquids other than simple water or glycerin, and which invariably contain alcohol; solutions of volatile substances in alcohol are always termed spirits or essences. While tinctures are usually assumed to be solutions of vegetable principles, this is not the case in all the official tinctures; two of these, the tinctures of iodine and ferric chloride, are solutions of inorganic substances. Tincture of iodine is also an exception to the rule that tinctures are solutions of non-volatile substances. The menstruum or solvent used in the preparation of tinctures may be simply alcohol, various mixtures of alcohol and water, or of alcohol, glycerin, and water, ammoniated alcohol in the form of aromatic spirit of ammonia, and mixtures of alcohol and ether; according as these different menstrua are employed, tinctures are divided into groups designated as alcoholic, hydro-alcoholic, ammoniated, and ethereal tinctures respectively. Ethereal tinctures are not recognized in our Pharmacopœia, but are employed to some extent in Europe.

The Pharmacopœia recognizes seventy-two tinctures, of which twenty are made with alcohol alone, fifty with a hydro-alcoholic menstruum, and two with ammoniated alcohol; from this it is seen that the tendency is in the direction of weaker alcohol, and many tinctures formerly made with alcohol exclusively, are now found equally efficient and permanent when made with a mixture of alcohol and water. The valuable solvent and preservative properties of alcohol have been explained in a former chapter; these are retained in the various hydro-alcoholic mixtures, in which the proportions of alcohol and water are so adjusted that complete extraction of the valuable constituents of the drug is insured as well as permanence of the solution; the solution of much inert and unstable matter is likewise thus avoided. Tinctures made with weak alcohol are also more readily miscible with aqueous liquids—a point often of great value in dispensing medicines. The addition of glycerin to the menstruum is frequently desirable to facilitate the perfect extraction of astringent and other principles and prevent subsequent changes in the finished tincture, due to atmospheric influences, which cause the gelatinization of the solution or deposit of unsightly precipitates.

Tinctures are, as a rule, prepared by percolation, except in the case of a few resins, balsams, gum-resins, and extractive drugs, for which maceration has proven more satisfactory. The process of per-

colation has been fully described on page 124 *et seq.*, as well as the precautions necessary to insure perfect extraction of drugs. The great advantages to be derived from a proper moistening and preliminary maceration of the drug have been already pointed out in the chapter on Percolation. The value of this mode of solution cannot be overestimated in the preparation of tinctures, and as the amount of available menstruum is ample, complete exhaustion of the drug will have been effected before all the solvent has passed through; the objection urged that menstruum is retained by the marc, can be easily overcome (see page 129), and is but trifling as compared with the gain in time and in the perfect, clear solution at once obtained.

Of the seventy-two official tinctures, fifty-six, or over three-fourths of the whole number, are directed to be made by percolation, eleven by maceration, four by direct solution, and one by decoction and subsequent concentration. In the pharmacopœial titles of tinctures, the names of the drugs furnishing the active ingredients are indicated in all but twelve; of these, six are officially designated as *compound tinctures*, namely: the *compound tincture* of *benzoin*, *cardamom*, *catechu*, *cinchona*, *gentian*, and *lavender*. In the remaining six titles, only the name of the chief ingredient is mentioned; as *tincture of aloes*, *tincture of cinnamon*, *camphorated tincture of opium*, *tincture of rhubarb*, *sweet tincture of rhubarb*, and *aromatic tincture of rhubarb*.

Upon exposure to air and light, tinctures, like all vegetable solutions, are apt to undergo change, and should, therefore, be kept in well-closed containers, in shady places; extremes of temperature are equally hurtful, on account of the possible change in the menstruum. Fortunately, the deposits formed in tinctures consist, as a rule, only of inert extractive matter, which may be removed by filtration.

The following table shows at a glance the composition and strength of the official tinctures, as well as the fineness of powder and the menstruum used in their preparation.

Table of Official Tinctures arranged Alphabetically.

Tinctures Made by Percolation.

Official Name.	Quantity of drug used for 1000 Cc. of tincture.	Fineness of powder.	Menstruum.	Quantity of menstruum to moisten drug.	Degree of Packing.
Tinctura—					
Aconiti . . .	Aconite 350 Gm.	No. 60	Alcohol 7 vols. Water 3 "	200 Cc.	Firm.
Aloes	Purified Aloes 100 " Liquorice Root 200 "	" 40	Dil. Alcohol	80 "	"
Aloes et Myrrha	Purified Aloes 100 " Myrrh 100 " Liquorice Root 100 "	" 40	Alcohol 3 vols. Water 1 vol.	60 "	"
Arnicæ Florum	Arnica Flowers 200 "	" 20	Dil. Alcohol	0	"
Arnicæ Radicis	Arnica Root 100 "	" 40	Alcohol 65 vols. Water 35 "	150 "	"
Aurantii Amari	Bitter Orange Peel 200 "	" 30	Alcohol 6 " Water 4 "	200 "	Moderate.
Aurantii Dulcis	Sweet Orange Peel 200 "	Cut in small pieces	Alcohol	800 "	"
Belladonnæ Fol.	Belladonna Leaves 150 "	No. 60	Dil. Alcohol	200 "	Firm.
Bryoniæ . .	Bryonia 100 "	" 40	Alcohol	100 "	"
Calendulæ . .	Calendula 200 "	" 20	Alcohol	200 "	"
Calumbæ . .	Calumba 100 "	" 20	Alcohol 6 vols. Water 4 "	100 "	"
Cannabis Indicæ	Indian Cannabis 150 "	" 40	Alcohol	150 "	"
Cantharidis	Cantharides 50 "	" 60	Alcohol	30 "	"
Capsici	Capsicum 50 "	" 30	Alcohol 95 vols. Water 5 "	40 "	"
Cardamomi . .	Cardamom 100 "	" 30	Dil. Alcohol	100 "	"
Cardamomi Composita	Cardamom 20 " Cassia Cinnamon 20 " Caraway 10 " Cochineal 5 " (the finished product also contains 5 per cent of glycerin, added after percolation)	" 40	Dil. Alcohol	25 "	"
Catechu Composita	Catechu 100 Gm. Cassia Cinnamon 50 "	" 40	Dil. Alcohol	0	"
Chiratæ	Chirata 100 "	" 40	Alcohol 65 vols. Water 35 "	100 "	"
Cimicifugæ . .	Cimicifuga 200 "	" 60	Alcohol	150 "	"
Cinchonæ . .	Cinchona 200 "	" 60	Alcohol 67.5 vols. Water 25 " Glycerin 7.5 "	200 "	"
Cinchonæ Composita	Red Cinchona 100 " Bitter Orange Peel 80 " Serpentaria 20 "	" 60	Alcohol 85 " Water 7.5 " Glycerin 7.5 "	200 "	"
Cinnamomi . .	Ceylon Cinnamon 100 "	" 40	Alcohol 75 " Water 20 " Glycerin 5 "	50 "	"
Colchici Seminis	Colchicum Seed 150 "	" 30	Alcohol 6 vols. Water 4 "	100 "	Moderate.
Croci	Saffron 100 "	.....	Dil. Alcohol	100 "	Firm.
Cubebæ . . .	Cubeb 200 "	" 30	Alcohol	100 "	"
Digitalis . . .	Digitalis 150 "	" 60	Dil. Alcohol	150 "	"
Gallæ	Nutgall 200 "	" 40	Alcohol 9 vols Glycerin 1 vol.	0	"
Gelsemii . . .	Gelsemium 150 "	" 60	Alcohol 65 vols. Water 35 "	100 "	"
Gentianæ Composita	Gentian 100 " Bitter Orange Peel 40 " Cardamom 10 "	" 40	Alcohol 6 " Water 4 "	100 "	Firm.
Humuli . . .	Hops 200 "	" 20	Dil. Alcohol	400 "	"
Hydrastis . .	Hydrastis 200 "	" 60	Dil. Alcohol	150 "	"
Hyoscyami . .	Hyoscyamus 150 "	" 60	Dil. Alcohol	150 "	"
Krameriæ . . .	Krameria 200 "	" 40	Dil. Alcohol	200 "	"
Lactucarii . .	Lactucarium 500 " (the drug is mixed with sand and treated twice with benzin, before percolation)	.....	Alcohol 50 vols. Water 20 " Glycerin 25 " afterward Dil. Alcohol	0	Moderate.

Official Name.	Quantity of drug used for 1000 Cc. of tincture.	Fineness of powder.	Menstruum.	Quantity of menstruum to moisten drug.	Degree of Packing.
Tinctura—Lavandulæ Composita	Oil of Lavender Flowers 8 Cc. Oil of Rosemary 2 " Cassia Cinnamon 20 Gm. Cloves 5 " Nutmeg 10 " Red Saunders 10 "	No. 20	Alcohol 70 vols. Water 25 " afterward Dil. Alcohol	...	Firm.
Lobeliæ . . .	Lobelia 200 "	" 40	Dil. Alcohol	200 Cc.	"
Matico . . .	Matico 100 "	" 40	Dil. Alcohol	100 "	"
Opii	Powd. Opium 100 "	.....	Dil. Alcohol		
Opii Deodorata	Powd. Opium 100 "	.....	Water	Finished product contains 20 per cent. of alcohol	
Physostigmatis	Physostigma 150 "	" 40	Alcohol	100 Cc.	Firm.
Pyrethri . . .	Pyrethrum 200 "	" 40	Alcohol	150 "	"
Quassiæ . . .	Quassia 100 "	" 40	Alcohol 35 vols. Water 65 "	100 "	"
Rhei	Rhubarb 100 " Cardamom 20 "	" 40	Alcohol 6 " Water 3 " Glycerin 1 vol.	100 "	"
Rhei Aromatica	Rhubarb 200 " Cassia Cinnamon 40 " Cloves 40 " Nutmeg 20 "	" 40	Alcohol 5 vols. Water 4 " Glycerin 1 vol. afterward Dil. Alcohol	100 "	"
Rhei Dulcis . .	Rhubarb 100 " Glycyrrhiza 40 " Anise 40 " Cardamom 10 "	" 40	Alcohol 5 vols. Water 4 " Glycerin 1 vol. afterward Dil. Alcohol	150 "	"
Sanguinariæ .	Sanguinaria 150 "	" 60	Alcohol 6 vols. Water 4 " Acetic Acid 2 p c.	100 "	"
Scillæ	Squill 150 "	" 30	Alcohol 3 vols. Water 1 vol.	200 "	"
Serpentariæ .	Serpentaria 100 "	" 40	Alcohol 65 vols. Water 35 "	100 "	"
Stramonii Seminis	Stramonium Seed 150 "	" 40	Dil. Alcohol	100 "	"
Strophanthi	Strophanthus 50 "	" 30	Alcohol 65 vols. Water 35 "	70 "	"
Sumbul . . .	Sumbul 100 "	" 30	Alcohol 65 " Water 35 "	100 "	"
Valerianæ . .	Valerian 200 "	" 60	Alcohol 75 " Water 25 "	100 "	"
Valerianæ Ammoniata	Valerian 200 "	" 60	Aromatic Spirit of Ammonia	200 "	"
Vanillæ . . .	Vanilla 100 "	.....	Alcohol 65 vols. Water 35 "		
Veratri Viridis	Veratrum Viride 400 "	" 60	Alcohol	150 "	"
Zingiberis . .	Ginger 200 "	" 40	Alcohol	50 "	"

Tinctures Made by Solution.

Official Name.	Quantity of drug used for 1000 Cc. of tincture.	Menstruum.
Tinctura—		
Ferri Chloridi . . .	Solution of Ferric Chloride . . 250 Cc.	Alcohol.
Ipecacuanhæ et Opii .	Fluid Extract of Ipecac . . . 100 " Tincture of deodorized Opium . 1000 "	Dil. alcohol.
Iodi	Iodine . . . . . 70 Gm	Alcohol.
Nucis Vomicæ	Extract of Nux Vomica . . . 20 "	Alcohol 750 Cc. Water 250 "

Tinctures Made by Maceration.

Official Name.	Quantity of drug used for 1000 Cc. of tincture.	Menstruum.	Length of time of maceration.
Tinctura—			
Asafœtidæ	Asafetida, bruised 200 Gm.	Alcohol	7 days.
Benzoini	Benzoin, coarse powder 200 "	"	7 "
Benzoini Composita	Benzoin, " " 120 " Purified Aloes 20 " Storax 80 " Balsam of Tolu 40 "	"	2 hours; digestion at a temperature of 65°C. (149° F.)
Herbarum Recentium	Fresh Herbs (bruised) 500 "	"	14 days.
Guaiaci	Guaiac, coarse powder 200 "	"	7 "
Guaiaci Ammoniata	Guaiac, coarse powder 200 "	Aromatic Spirit of Ammonia Glycerin 150 Cc. Water 200 " Alcohol 650 "	7 " 24 hours.
Kino	Kino 100 "		
Moschi	Musk 50 "	Dil. Alcohol	7 days.
Myrrhæ	Myrrh, moderately coarse powder 200 "	Alcohol	7 "
Opii Camphorata	Opium powdered 4 " Benzoic Acid 4 " Camphor 4 " Oil of Anise 4 Cc. Glycerin 40 "	Dil. Alcohol.	3 "
Tolutana	Balsam of Tolu 100 Gm.	Alcohol	Until dissolved.

Tincture Made by Decoction.

Official Name.	Quantity of drug used for 1000 Cc. of tincture.	Menstruum.
Tinctura Quillajæ	Quillaja, coarsely ground 200 Gm.	Boiling water; the decoction is preserved by alcohol, of which the finished tincture contains 35 per cent.

The strength of the tinctures of the U. S. Pharmacopœia varies from 1.6 to 50 Gm. of drug, being in the majority of cases 10, 15, or 20 Gm. for every 100 Cc. of finished product, while the British Pharmacopœia, as a rule, employs 2½ oz. av. of the drug for each Imperial pint (20 fluidounces) of tincture, or 1 part of drug for 8 measured parts of fluid. The French and German Pharmacopœias prepare their tinctures, almost without exception, of such strength that 1 part of drug is represented by about 5 or 10 parts of tincture by weight. While the difference in strength between our own and the British tinctures, is in the majority of cases, of no great importance, it is quite marked in a few tinctures, and should be borne in mind when filling British prescriptions; thus, our tincture of aconite is about 3 times as strong as the British tincture, our tincture of cantharides is 4 times as strong, our tincture of belladonna is 3 times as strong, our tincture of iodine nearly 3 times as strong, our tincture of opium ⅓ stronger, our tincture of nux vomica about 50 per cent. stronger, and our tincture of veratrum viride twice as strong. The following table represents a classification of the official tinctures based upon the amount of drug represented in each liter.

TABLE OF OFFICIAL TINCTURES ARRANGED ACCORDING TO STRENGTH.

16 Gm. of Drug in 1000 Cc.	Tinctura Opii Camphorata.
	" Cantharidis.
	" Capsici.
50 Gm. of Drug in 1000 Cc.	" Moschi.
	" Strophanthi.
	" Cardamomi Composita.
55 Gm. of Drug in 1000 Cc.	" Lavandulæ.
70 Gm. of Drug in 1000 Cc.	" Iodi.
	" Arnicæ Radicis.
	" Bryoniæ.
	" Calumbæ.
	" Cardamomi.
	" Chiratæ.
	" Cinnamomi.
	" Croci
	" Kino.
100 Gm. of Drug in 1000 Cc.	" Matico.
	" Opii.
	" Opii Deodorata.
	" Quassiæ.
	" Serpentariæ.
	" Sumbul.
	" Tolutana.
	" Vanillæ.
120 Gm. of Drug in 1000 Cc	" Rhei.
131 Gm of Drug in 1000 Cc.	" Ferri Chloridi.
(Calculated for anhydrous salt.)	" Belladonnæ Foliorum.
	" Cannabis Indicæ.
	" Catechu Composita.
	" Colchici Seminis.
	" Digitalis.
	" Gelsemii.
150 Gm. of Drug in 1000 Cc.	" Gentianæ Composita.
	" Hyoscyami.
	" Physostigmatis.
	" Rhei Dulcis.
	" Sanguinariæ.
	" Scillæ.
	" Stramonii Seminis
	" Arnicæ Florum.
	" Asafœtidæ.
	" Aurantii Amari.
	" Aurantii Dulcis.
	" Benzoini.
	" Calendulæ.
	" Cimicifugæ.
	" Cinchonæ.
	" Cinchonæ Composita.
	" Cubebæ.
	" Gallæ.
200 Gm. of Drug in 1000 Cc.	" Guaiaci.
	" Guaiaci Ammoniata.
	" Humuli
	" Hydrastis
	" Ipecacuanhæ et Opii.
	" Krameriæ.
	" Lobeliæ.
	" Myrrhæ.
	" Pyrethri.
	" Quillajæ.
	" Valerianæ.
	" Valerianæ Ammoniata.
	" Zingiberis.

260 Gm of Drug in 1000 Cc.	Tinctura Benzoini Composita.
300 Gm. of Drug in 1000 Cc.	" Aloes.
	" Aloes et Myrrhæ.
	" Rhei Aromatica.
350 Gm. of Drug in 1000 Cc.	" Aconiti
400 Gm. of Drug in 1000 Cc.	" Veratri Viridis.
500 Gm. of Drug in 1000 Cc.	" Herbarum Recentium.
	" Lactucarii.

Special Remarks.

Tinctura Aconiti. This important tincture requires care in its preparation, as the drug is not easily exhausted. The drug should be of prime quality, producing, when chewed, the characteristic tingling sensation in the tip end of the tongue, and the percolation should be conducted slowly at the rate of not over 10 drops per minute. The residue in the percolator must be devoid of all physiological effect.

Fleming's tincture of aconite, which is still prescribed by some physicians, is very nearly twice as strong as the official tincture; it is made with alcohol, and 480 grains of aconite root are represented in 1½ fluidounces of the tincture.

Tinctura Aloes. The use of powdered liquorice root enables the tincture to be made by percolation, which otherwise would be impossible; the liquorice also modifies the bitter taste of the aloes considerably. The same remarks apply to the tincture of aloes and myrrh.

Tinctura Arnicæ Florum. The pharmacopœial direction to pack the powder dry, offers no advantage in the preparation of the tincture; if the powder be moistened with about 1½ times its weight of menstruum it can be more firmly compressed than when dry.

Tinctura Asafœtidæ. Select asafetida should be used, containing at least 60 per cent. of matter soluble in alcohol. It must be frequently agitated during maceration.

Tinctura Aurantii Dulcis. Since the inner white layer of the orange peel contains tannin and is devoid of aroma, it should be carefully removed with a sharp knife, and only the yellow outer rind of the fresh peel be used, as officially directed; this can be split into narrow strips and then cut into small pieces, or the rind may be carefully grated. Maceration for five or six days, with frequent agitation, is advantageous, as packing of the pieces is performed with difficulty.

Tinctura Benzoini Composita. This tincture is intended to take the place of numerous proprietary preparations, such as Wade's, Vervain's, Saint Victor's, Jesuits', Friar's, Turlington's, Persian and Swedish balsam.

Tinctura Bryoniæ. The official directions to employ recently dried bryony root will be found difficult to follow, since bryony does not grow in this country. Bryony is known to yield its active virtues to water; diluted alcohol will, therefore, produce a tincture as efficient as one made according to the Pharmacopœia, with alcohol.

Tinctura Cannabis Indicæ. The tincture of the British Pharmacopœia is nearly three times as strong as our own, being made by dis-

solving 1 oz. av. of the extract of Indian hemp in 20 fluidounces of alcohol.

Tinctura Cinnamomi. The tendency to gelatinize, which has been observed in tincture of cinnamon when made with weak alcohol, has been overcome in the Pharmacopœia by the use of a stronger alcoholic menstruum and the addition of glycerin.

Tinctura Ferri Chloridi. When an acid solution of ferric chloride and alcohol are mixed, as in the official process, an ethereal odor is gradually developed, due to chemical action between the alcohol and the acid; the pharmacopœial direction, to allow the mixture to stand at least three months before using, is intended to insure uniformity by bringing all changes to completion. When exposed to light, the ferric chloride is, in part, reduced to the ferrous condition; hence the necessity for protecting the tincture from light.

Tinctura Gallæ. Tincture of nutgall, when kept on hand for some time, undergoes change and deposits gallic acid; the presence of glycerin retards such changes.

Tinctura Herbarum Recentium. Tinctures of fresh herbs can, of course, only be made from such plants as grow in this country, and must vary in quality according to the amount of moisture present in the drug; the use of alcohol as a menstruum prevents the solution of mucilaginous and other inert matter and insures the presence of all valuable alcohol-soluble constituents, such as alkaloids, resins, volatile oils, etc.

Tinctura Ipecacuanhæ et Opii. This preparation may be regarded as a liquid form of Dover's powder, as it represents, in each Cc., the equivalent of 0.100 Gm. each of ipecac and opium. The concentration of the tincture of deodorized opium is necessary for the introduction of the fluid extract of ipecac, the original volume being again restored by addition of diluted alcohol; the precipitate formed consists of inert matter and is removed by filtration.

Tinctura Kino. The tendency of this tincture to gelatinize can be entirely overcome by preserving it in a cool place, in well-stoppered 1 oz. or 2 oz. vials, thus obviating frequent exposure to air.

Tinctura Lactucarii. Lactucarium contains, besides the active bitter principles *lactucin*, *lactucic acid*, and *lactucopicrin*, an inert caoutchouc-like substance, lactucerin, which is removed by treatment with benzin, as directed in the Pharmacopœia; the mixture must be filtered in a well-covered funnel and the dregs carefully washed with benzin. In order to get rid of all benzin odor, the residue should be dried in a current of warm air. The percolation of the powder, mixed with sand, presents no difficulty, as the active principles are all soluble in the official menstruum, but in order to insure complete exhaustion, the percolate should be collected in drops, very slowly.

Tinctura Moschi. Musk will yield to water about 50 or 60 per cent. of its weight of soluble matter, whereas alcohol extracts only about 10 per cent.; the official mode of manipulation can be advantageously modified by macerating the musk with the water, for twelve

hours, before adding the alcohol. The persistent odor of musk can be removed from mortars and graduates by means of quinine or powdered ergot, made into a soft paste with water and spread over the surface of the apparatus.

Tinctura Nucis Vomicæ. The present official formula is very simple and insures a tincture of uniform strength, containing 0.003 Gm. of mixed alkaloids in each Cc.

Tinctura Opii. Although the Pharmacopœia directs the use of powdered opium, for the sake of uniformity, a somewhat coarser state of division is preferable, and percolation to complete exhaustion can be carried on more satisfactorily with opium in No. 40 powder. The preliminary digestion with water, for twelve hours, prepares the soluble principles for better extraction with the diluted alcohol, and a somewhat coarser powder prevents compaction of the mass. The insoluble calcium phosphate is intended to facilitate the percolation of the fine powder, but does this very imperfectly. Official tincture of opium must contain from 0.013 to 0.015 Gm. of crystallized morphine in each Cc.

Tinctura Opii Deodorata. The active virtues of opium can be completely extracted with water; the maceration for twelve hours should, however, be accompanied by frequent agitation, and subsequent percolation continued until the liquid passes but slightly imbued with the peculiar taste of opium. The treatment of the concentrated percolate with ether, as directed in the Pharmacopœia, is intended to remove a peculiar odorous principle and narcotine, which it does very effectually, but if the official *modus operandi* be strictly followed—namely, to shake the ether repeatedly with the aqueous solution—a very annoying and persistent emulsion will generally result. A much better plan is to add the ether to the liquid in a cylinder or large globular separator and bring the two fluids into intimate contact, either by slowly inverting the cylinder or by rotating the separator; this treatment should be continued for some time, and repeated frequently during twelve or twenty-four hours. The aqueous fluid should then be carefully separated, either by being drawn off or by decanting or siphoning off the ether, and the washing with ether repeated, this time using about one-half as much ether as before.

Experiments made with benzene and petroleum benzin as deodorizing agents have proven their inferiority to ether, mainly on account of their own disagreeable and rather persistent odor. In my experience, the most satisfactory plan is to deodorize the powdered opium itself with ether, by treating it three times after the manner prescribed in the Pharmacopœia for "Opium Deodoratum," and then to exhaust this thoroughly with water, concentrate the percolate to four-fifths of the intended volume of finished product, and add the necessary quantity of alcohol; this method involves the use of a larger quantity of ether (which can be redistilled and used for a subsequent operation), but entirely obviates the formation of troublesome emulsions, and yields an unobjectionable product.

Federer's process for deodorizing opium by freezing an aqueous infusion, which was published in full in the *Druggists' Circular* for April, 1887, is economical and not very troublesome; it removes all odor and narcotine, but I have also invariably noticed a loss of morphine when operating with assayed opium. The marc was carefully tested and found completely free from morphine, proving that the loss occurred in the dark deposit separated during the freezing operation.

The morphine strength of this tincture is identical with that of the plain tincture of opium.

Tinctura Physostigmatis. Tincture of Calabar bean should be preserved in small, well-stoppered vials, protected against light, on account of the sensitiveness of the alkaloidal salts, when in solution, to the influence of air and light.

Tinctura Quassiæ. No tannin being contained in quassia, the tincture is not discolored by iron salts, and is often selected from among the bitter stomachics on that account.

Tinctura Quillajæ. Boiling water extracts all the saponaceous principles from quillaja, but also considerable inert matter, which is sought to be removed, in the official process for making the tincture, by addition of alcohol; the latter also finally preserves the finished product.

Tinctura Sanguinariæ. The addition of acetic acid to the menstruum not only facilitates the exhaustion of the drug, but also materially improves the stability of the tincture.

Tinctura Strophanthi. Strophanthus seeds contain considerable fixed oil, which can be removed by percolation with ether, before using the official menstruum; ether does not affect the active principle strophanthin, which is perfectly soluble in diluted alcohol.

CHAPTER XXI.

WINES AND VINEGARS.

THESE two classes of preparations have almost passed into disuse among physicians, and their number has been diminished in the last Pharmacopœia; in place of thirteen wines officially recognized in 1880, only ten now remain, and the number of vinegars has been reduced from four to two.

Wines.

Both white and red wines are recognized in the Pharmacopœia, but in the preparation of the official medicated wines, only the white wine is directed, on account of its lesser astringency, and in each case the alcoholic strength of the preparation is increased by the addition of alcohol to the extent of 15 per cent. This fortification of the wine is particularly necessary to insure the stability of vegetable solutions during warm weather. Native wines can now be obtained of good quality, and are given preference by the Pharmacopœia. The chief difference between white and red wines lies in the dark coloring matter and larger proportion of tannin in the latter, due to the fact that, in the case of red wines, the pericarp, or skin of the grape, is allowed to remain with the expressed juice during fermentation; were the skins carefully removed, many dark-colored grapes would also yield white wines, for the juice is naturally colorless. Much of the tannin found in wines may also be derived from the casks in which they are stored. As white wines, as a rule, contain only very small proportions of tannin, they are preferred as menstrua for medicated wines.

The process of freeing wines from tannin is termed detannating them, and may be effected by adding to the wine either some freshly-prepared ferric hydroxide or some sweet milk; the former plan is the most effectual, although the most laborious, but should not be employed if the wine is wanted entirely free from iron, some of which goes into solution. As the removal of tannin from wine in no way interferes with its quality—alcoholic strength and aroma remaining the same, and only coloring matter being lost—a supply of detannated wine should be kept on hand, for it requires very little more labor to detannate a gallon than a pint. Wines containing tannin are not well suited for use with alkaloidal drugs, iron salts, antimony compounds, etc., as precipitates will be gradually formed and deposited. The detannating agent must be allowed to remain in

contact with the wine for some days, with occasional agitation, until a few drops of tincture of ferric chloride, added to a small portion of the wine, no longer produce a dark color.

If ferric hydroxide is to be used, it must be freshly prepared, and a convenient quantity then be added to the wine—about 8 ounces of the expressed, but moist, precipitate to a gallon. Sweet milk may be employed in the proportion of 4 fluidounces to a gallon.

Both white and red wines have an acid reaction, due to potassium bitartrate held in solution; this acidity is limited, by the Pharmacopœia, to from 4.49–7.78 Gm. of free acid per liter. The amount of solid matter in wines should range between 1.5 and 3.5 per cent., and may be ascertained by evaporation and drying on the water-bath during twelve hours. The Pharmacopœia also specifies the alcoholic strength to be from 10–14 per cent. by weight, which is equal to 12.4–17.3 per cent. by volume of absolute alcohol, the official directions for ascertaining the percentage of alcohol present being to take the specific gravity of the wine at 15.6° C. (60° F.), evaporate a carefully measured portion of it, in a tared capsule, to one-third of its weight, cool and restore the original volume by the addition of water, and again take the specific gravity of the liquid at 15.6° C. (60° F.); the difference between the two specific gravities subtracted from 1.000, indicates the specific gravity of an alcohol containing the same percentage of absolute alcohol as the wine, the corresponding percentage being ascertained by reference to the alcoholometric tables published in the Pharmacopœia. Suppose the wine before evaporation has a specific gravity of 0.9930, and after evaporation and addition of water, 1.0098, then $1.0098 - 0.9930 = 0.0168$, and $1.000 - 0.0168 = 0.9832$; by referring to the tables it is found that alcohol of 0.9832 specific gravity at 15.6° C. (60° F.) contains between 10 and 11 per cent. by weight, or between 12 and 13 per cent. by volume, of absolute alcohol.

Red wines are frequently colored artificially with aniline, which coloration may be detected by the tests officially directed for that purpose. If red wine be mixed with twice its volume of potassa solution and a small quantity of chloroform, and the mixture then carefully heated, the presence of certain aniline colors will develop a very disagreeable odor, due to the formation of isonitril. Fuchsine may be detected by the crimson color imparted to uncolored silk fibre placed in contact with a mixture of acetic acid and an ethereal extract of red wine previously treated with ammonia water in excess; as the mixture is evaporated in a porcelain dish, the color is developed. Hydrochloric acid should not produce red color if added to a filtrate obtained from shaking warm red wine with manganese dioxide, showing the absence of sulpho-fuchsine.

THE OFFICIAL MEDICATED WINES. Of these, two are prepared by percolation, two by maceration, and four by simple solution of the medicinal agent in the menstruum.

TABLE OF OFFICIAL WINES SHOWING STRENGTH AND MENSTRUUM USED.

Made by Percolation.

Official Name.	Quantity of drug used for 1000 Cc.	Fineness of Powder.	Menstruum.	Quantity of Menstruum used for moistening the drug.
Vinum— Colchici Radicis	Colchicum Root 400 Gm	No. 30	White Wine 850 Cc. Alcohol 150 "	100 Cc.
Ergotæ	Ergot 150 Gm.	No 30	White Wine 850 " Alcohol 150 "	40 Cc

Owing to the weak alcoholic menstruum, both drugs should be packed only moderately.

Made by Maceration.

Official Name.	Quantity of drug used for 1000 Cc.	Fineness of Powder.	Menstruum.	Length of time of Maceration.
Vinum— Colchici Seminis	Colchicum Seed 150 Gm.	No. 30	White Wine 850 Cc. Alcohol 150 "	7 days
Opii	Opium 100 Gm. Cinnamon 10 " Cloves 10 "	Fine Powder No. 60 No. 30	White Wine 850 " Alcohol 150 "	7 days.

Wine of opium is of the same morphine strength as the tincture, namely, 0.013–0.015 Gm. in each Cc.

Made by Simple Solution.

Official Name.	Composition.	
Vinum Antimonii	Antimony and Potassium Tartrate	4 Gm.
	Boiling Distilled Water	65 Cc.
	Alcohol	150 "
	White Wine, sufficient to make	1000 "
Vinum Ferri Amarum	Soluble Iron and Quinine Citrate	50 Gm.
	Tincture of Sweet Orange Peel	150 Cc.
	Syrup	300 "
	White Wine, sufficient to make	1000 "
Vinum Ferri Citratis	Iron and Ammonium Citrate	40 Gm.
	Tincture of Sweet Orange Peel	150 Cc.
	Syrup	100 "
	White Wine, sufficient to make	1000 "
Vinum Ipecacuanhæ	Fluid Extract of Ipecac	100 "
	Alcohol	100 "
	White Wine	800 "

Vinegars.

The valuable solvent as well as preservative properties of diluted acetic acid, were at one time employed for a larger class of preparations than at present, of which the vinegar of opium and vinegar of squill alone are now recognized in the Pharmacopœia. The official diluted acetic acid is made by mixing one part of 36 per cent. acetic

acid with five parts of water, and contains, therefore, 6 per cent. of absolute acetic acid.

THE OFFICIAL VINEGARS. These are made by maceration and subsequent expression, and represent 10 Gm. of the drug in 100 Cc. of finished product.

Acetum Opii. Vinegar of opium is made by macerating 100 Gm. of powdered opium and 30 Gm. of nutmeg in No. 30 powder, with 500 Cc. of diluted acetic acid, for seven days, with frequent agitation; after expressing the liquid, the residue is mixed with 200 Cc. of diluted acetic acid and again expressed. After mixing and filtering the liquids, 200 Gm. of sugar are dissolved in the filtrate, and sufficient diluted acetic acid is added to bring the volume up to 1000 Cc.

Vinegar of opium is of the same morphine strength as the tincture and wine, containing 0.013 to 0.015 Gm. in each Cc.

Acetum Scillæ. Squill is readily exhausted by diluted acetic acid. The Pharmacopœia directs the use of a No. 30 powder, but as the drug swells considerably from absorption of the menstruum, a No. 20 powder will be preferable; 100 Gm. of squill are macerated with 900 Cc. of diluted acetic acid, for seven days, with occasional agitation, after which the mixture should be strained with expression, and the residue washed with sufficient diluted acetic acid to bring the volume of the strained liquid up to 1000 Cc. It will be found advantageous to set the strained liquid aside for three or four days before filtering it.

CHAPTER XXII.

FLUID EXTRACTS.

THE term fluid extract, in its present acceptation, is applied to concentrated alcoholic or hydro-alcoholic solutions of vegetable principles, which are permanent and represent all the active virtues of the drugs from which they are made; they are officially recognized in the Pharmacopœias of the United States, Great Britain, Germany, and Switzerland, differing but slightly in strength in the four countries.

Fluid extracts, or liquid extracts, as they are called in Great Britain, were first introduced about the year 1832; their origin, although generally credited to American pharmacy, belongs more probably to England, since in 1834 English fluid extracts were already known in this country. Prior to 1847 very little interest appears to have been taken in this class of preparations in the United States, only three fluid extracts being on record as in use at that time—namely, senna, valerian, and rhubarb; from that time forward, fluid extracts grew in favor, and the Pharmacopœia of 1850 gave working formulas for seven concentrated solutions, of which, however, only one—valerian—is deserving of the title of fluid extract in the present definition of that term; two were oleoresins, cubebs and black pepper, and four concentrated syrups, rhubarb, sarsaparilla, senna, and spigelia and senna. In 1860 the number of fluid extracts officially recognized was increased to *twenty-five*, in 1870 to *forty-six*, in 1880 to *seventy-nine*, and in the present (1890) edition of the Pharmacopœia *eighty-eight* are directed.

Prior to 1880 the strength of fluid extracts, as prescribed by the Pharmacopœia, was 1 grain of drug to 1 minim of fluid extract; since that time the pharmacopœial strength is based upon the relation of the metric measures of weight and capacity, so that any weight of a given drug is to be converted into a fluid extract having the bulk of the same weight of water at its maximum density, or, in other words, *one gramme* of the drug is represented by *one cubic centimeter* of the fluid extract. The present strength of official fluid extracts is about 5 per cent. weaker than formerly. British liquid extracts, with the exception of those of male fern, cinchona, opium, pareira, and liquorice, are of the strength of one avoirdupois ounce to one imperial fluidounce, which practically corresponds to our own. In Germany, each gramme of drug is represented by one gramme of fluid extract, the relation being weight for weight.

All the official fluid extracts are directed to be prepared by perco-

lation, a menstruum uniform in alcoholic strength being employed during the process of exhaustion. When, however, glycerin is used with the first portion of the menstruum, percolation is continued and finished with a liquid of the same alcoholic strength, but not mixed with glycerin; the only exception to this is in the case of fluid extract of wild cherry, where the drug is moistened and packed with a mixture of glycerin and water, and then percolated with alcohol and water. With the exception of castanea and triticum, a certain portion of the stronger percolate is set aside as a reserve, and the weaker percolate is directed to be evaporated to a soft extract, which is dissolved in the reserved portion, the requisite volume of finished product being made up with fresh menstruum containing no glycerin. By evaporating the weak percolate to a soft extract, most of the water is also expelled, and the comparatively small portion remaining with the extract will occasion but a slight change in the menstruum of the reserved portion, which, at the same time, is the best solvent for the extractive matter; finally, the addition of fresh menstruum will not change the alcoholic strength of the liquid.

It is important that the exhaustion of the drug be conducted as carefully as possible, so that the reserved portion may represent a solution of nearly the whole active virtues of the drug; with this end in view the rate of percolation for 1000 Gm. of drug should be adjusted to about 8 drops per minute, at which rate about 20 Cc. can be collected in an hour. In the hands of a careful operator handling such quantities as are given in the pharmacopœial formulas, the official process yields very satisfactory results, and the danger arising from evaporation of the weak percolate may well be disregarded, since from 90 to 95 per cent. of the active principles are most likely contained in the reserved portion, therefore, only a trifling proportion of the medicinal virtues of the drug will be subjected to heat.

The official directions for the preparation of fluid extracts are intended for the quantity of drug designated in the formulas, and must of necessity often be modified by manufacturers who operate upon hundreds of pounds at one time; fineness of powder, degree of packing and rate of percolation must be adapted to the quantity of material in hand. Manufacturers, in some cases, resort to repeated maceration and expression instead of percolation.

Special authority is given by the Pharmacopœia to employ, where it may be applicable, the process of repercolation without change of initial menstruum. This process, which is fully described on page 130, is followed by several manufacturers, and does away with the possibility of injury from application of heat. Repercolation is particularly adapted to the preparation of fluid extracts, and the only objection that can be urged against its use is the enforced necessity of carrying on hand a series of bottles containing weak percolates, for each fluid extract made; disregarding this annoying feature, the process is less troublesome than any other, and in the case of some drugs must yield fluid extracts of superior quality.

All fluid extracts, no matter how carefully made, will begin to deposit soon after they are completed, and this precipitation will continue for a varying length of time. The menstruum dissolves certain extractive principles which it is incapable of retaining in perfect solution afterward under all changes of temperature, and thus far no method is known to entirely prevent such separation, which is augmented by exposure to light, air, and heat. Fluid extracts prepared entirely without heat are less prone to deposit than when made by the official process, and in these the amount of precipitate is often found very trifling; happily frequent examinations of precipitates in fluid extracts have disclosed the fact that they consist chiefly of inert extractive matter, and therefore do not affect the medicinal value of the preparation. All freshly made fluid extracts should be set aside in well-stoppered glass vessels, in dark and moderately cool places, for a period of two or three months, before filtering and bottling them; this plan is universally followed by large manufacturers, and explains the absence, in many cases, of appreciable deposits. Pharmacists will find that fluid extracts can be made from select drugs, on a small scale, as perfectly as in large quantities, and simple appearance, so often misleading, is no criterion as to quality.

With the exception of the fluid extracts of castanea, nux vomica, triticum, and wild cherry, all the fluid extracts of the Pharmacopœia are prepared by the following general formula; the quantity of menstruum for moistening the drug, the degree of pressure to be used in packing, and the quantity of percolate to be set aside as reserve being specified in each case:

1000 *Gm. of the powdered drug of the prescribed degree of fineness are thoroughly moistened with a certain quantity of the initial menstruum and packed more or less firmly in a cylindrical percolator; the drug having been properly covered with a paper diaphragm, enough menstruum is poured on to completely saturate the powder and leave a stratum above it. When the liquid begins to drop from the percolator, close the lower orifice, and having closely covered the percolator to prevent evaporation, macerate for forty-eight hours. Then allow percolation to proceed slowly, gradually adding menstruum (alcohol or alcohol and water), until the drug is exhausted. Reserve the first* 700 *to* 900 *Cc. of the percolate, and evaporate the remainder, at a temperature not exceeding* 50° *C.* (122° *F.*), *to a soft extract; dissolve this in the reserved portion and add enough menstruum to make the fluid extract measure* 1000 *Cc.*

Exception
Triticum
Nux vom
Wild Cherr
Castanea

The concentration of the weak percolate is usually effected by distilling off the alcohol, in a suitable apparatus on a water-bath, and finally evaporating the liquid, in a porcelain capsule, to the proper consistence, preferably with constant stirring. The Pharmacopœia does not in every case specify the temperature for evaporation, but it is best to keep it always below 50° C. (122° F.), so as to avoid changes in the extractive, as far as possible.

Of the eighty-eight official fluid extracts, seventeen are made with

alcohol alone, two with alcohol and glycerin, twenty-one with diluted alcohol, forty-six with various mixtures of alcohol and water, or alcohol, water, and glycerin, and in two, water only is used as a menstruum, although the preparation is finally preserved with alcohol; altogether, sixteen contain glycerin. In the case of four drugs, conium, ergot, nux vomica, and sanguinaria, acetic acid is added to the initial menstruum, to facilitate the extraction of the alkaloidal principles present; in the case of senega and of glycyrrhiza, ammonia water is added to the solvent, to prevent gelatinization in the former fluid extract, and to insure complete solution of the sweet principle in the latter drug. Arranged according to the menstruum, the official fluid extracts may be divided into twenty-one classes, as follows:

17 Made with alcohol: Aromatic powder, buchu, calamus, cannabis indica, capsicum, cimicifuga, cubeb, gelsemium, ginger, grindelia, iris, kusso, lupulin, mezereum, savin, veratrum viride, xanthoxylum.

1 Made with alcohol 4 volumes, glycerin 1 volume: Cinchona.

1 Made with alcohol 3 volumes, glycerin 1 volume: Cotton-root bark.

5 Made with alcohol 4 volumes, water 1 volume: Belladonna root, eriodictyon, podophyllum, rhubarb, serpentaria.

15 Made with alcohol 3 volumes, water 1 volume: Aconite, arnica root, black-haw, calumba, eucalyptus, guarana, ipecac, leptandra, matico, squill, stramonium seed, valerian, viburnum opulus. Same menstruum with addition of acetic acid: Nux vomica, sanguinaria.

8 Made with alcohol 2 volumes, water 1 volume: Bitter orange peel, chirata, colchicum root, colchicum seed, digitalis, hyoscyamus, menispermum, phytolacca root.

20 Made with diluted alcohol: Asclepias, chimaphila, coca, convallaria, cypripedium, dulcamara, eupatorium, gentian, lappa, lobelia, pilocarpus, rhamnus purshiana, rumex, scoparius, scutellaria, senna, spigelia, stillingia, taraxacum. Same menstruum with addition of acetic acid: Conium, ergot.

5 Made with alcohol 5 volumes, water 8 volumes: Frangula.

Made with alcohol 1 volume, water 2 volumes: Quassia, sarsaparilla.

1 Made with alcohol 72 volumes, water 18 volumes, glycerin 10 volumes: Pareira.

1 Made with alcohol 65 volumes, water 25 volumes, glycerin 10 volumes: Apocynum.

3 Made with alcohol 6 volumes, water 3 volumes, glycerin 1 volume: Aspidosperma, hydrastis, rubus.

4 Made with diluted alcohol 9 volumes, glycerin 1 volume: Geranium, krameria, rhus glabra, red rose.

1 Made with alcohol 5 volumes, water 8 volumes, glycerin, 1 volume: Hamamelis.

1 Made with alcohol 3 volumes, water 6 volumes, glycerin 1 volume: Sarsaparilla (compound fluid extract).

/ Made with alcohol 2 volumes, water 5 volumes, glycerin 3 volumes: Uva ursi.

/ Made with alcohol 75 volumes, water 20 volumes, ammonia water 5 volumes: Senega.

/ Made with alcohol 30 volumes, water 65 volumes, ammonia water 5 volumes: Glycyrrhiza.

/ Made with water 2 volumes, glycerin 1 volume, followed by a mixture of alcohol 85 volumes, water 15 volumes: Wild cherry.

/ Made with boiling water: Triticum. The finished product contains about 25 per cent. by volume of alcohol.

/ Made with boiling water and cold water: Castanea. The finished product contains 10 per cent. by volume of glycerin and about 20 per cent. by volume of alcohol.

Alphabetical List of Official Fluid Extracts,

Showing the fineness of powder, menstruum, degree of moisture, and reserve percolate directed by the Pharmacopœia.

Name.	Fineness of powder.	Initial Menstruum.	Quantity of Menstruum to moisten 1000 Gm. of the drug.	Reserve.
Fluid Extract of—				
Aconite	No. 60	Alcohol 750 Cc., Water 250 "	400 Cc.	900 Cc.
Apocynum	" 60	Alcohol 650 ", Glycerin 100 ", Water 250 "	400 "	900 "
Arnica Root	" 60	Alcohol 750 ", Water 250 "	400 "	900 "
Aromatic Powder	.....	Alcohol	350 "	850 "
Asclepias	No. 60	Diluted Alcohol	400 "	900 "
Aspidosperma	" 60	Alcohol 600 Cc., Glycerin 100 ", Water 300 "	400 "	800 "
Belladonna Root	" 60	Alcohol 800 ", Water 200 "	350 "	900 "
Bitter Orange Peel	" 40	Alcohol 600 ", Water 300 "	350 "	800 "
Buchu	" 60	Alcohol	400 "	850 "
Calamus	" 60	Alcohol	350 "	900 "
Calumba	" 20	Alcohol 750 Cc., Water 250 "	300 "	700 "
Cannabis Indica	" 20	Alcohol	300 "	900 "
Capsicum	" 60	Alcohol	500 "	900 "
Castanea	" 30	Boiling Water followed by Cold Water		
Chimaphila	" 30	Diluted Alcohol	400 "	700 "
Chirata	" 30	Alcohol 600 Cc., Water 300 "	350 "	850 "
Cimicifuga	" 60	Alcohol	250 "	900 "
Cinchona	" 60	Alcohol 800 Cc., Glycerin 200 "	350 "	750 "
Coca	" 40	Diluted Alcohol	430 "	800 "
Colchicum Root	" 60	Alcohol 600 Cc., Water 300 "	350 "	850 "
Colchicum Seed	" 30	Alcohol 600 ", Water 300 "	300 "	850 "
Conium	" 40	Diluted Alcohol 980 ", Acetic Acid 200 "	300 "	900 "
Convallaria	" 60	Diluted Alcohol	400 "	800 "
Cotton Root Bark	" 30	Alcohol 750 Cc., Glycerin 250 "	500 "	700 "
Cubeb	" 60	Alcohol	400 "	900 "
Cypripedium	" 60	Diluted Alcohol	400 "	900 "
Digitalis	" 60	Alcohol 600 Cc., Water 300 "	400 "	850 "
Dulcamara	" 60	Diluted Alcohol	400 "	800 "

Name.	Fineness of powder.	Initial Menstruum.	Quantity of Menstruum to moisten 1000 Gm. of the drug.	Reserve.
Fluid Extract of—				
Ergot	No. 60	Diluted Alcohol 980 Cc. Acetic Acid 20 "	300 Cc.	850 Cc.
Eriodictyon	" 60	Alcohol 800 " Water 200 "	400 "	900 "
Eucalyptus	" 40	Alcohol 750 " Water 250 "	400 "	900 "
Eupatorium	" 40	Diluted Alcohol	400 "	800 "
Frangula	" 40	Alcohol 500 Cc. Water 800 "	350 "	800 "
Gelsemium	" 60	Alcohol	300 "	900 "
Gentian	" 30	Diluted Alcohol	350 "	800 "
Geranium	" 30	Diluted Alcohol 900 Cc. Glycerin 100 "	350 "	700 "
Ginger	" 40	Alcohol	250 "	900 "
Glycyrrhiza	" 40	Alcohol 300 Cc. Ammonia Water 50 " Water 650 "	350 "	750 "
Grindelia	" 30	Alcohol	300 "	850 "
Guarana	" 80	Alcohol 750 Cc. Water 250 "	200 "	800 "
Hamamelis	" 40	Alcohol 500 " Glycerin 100 " Water 800 "	350 "	850 "
Hydrastis	" 60	Alcohol 600 " Glycerin 100 " Water 300 "	300 "	850 "
Hyoscyamus	" 60	Alcohol 600 " Water 300 "	400 "	900 "
Ipecac	" 80	Alcohol 750 " Water 250 "	350 "	900 "
Iris	" 60	Alcohol	400 "	900 "
Kousso	" 40	Alcohol	400 "	900 "
Krameria	" 30	Diluted Alcohol 900 Cc. Glycerin 100 "	400 "	700 "
Lappa	" 60	Diluted Alcohol	400 "	800 "
Leptandra	" 60	Alcohol 750 Cc. Water 250 "	400 "	800 "
Lobelia	" 60	Diluted Alcohol	350 "	850 "
Lupulin	.....	Alcohol	200 "	700 "
Matico	" 40	Alcohol 750 Cc. Water 250 "	300 "	850 "
Menispermum	" 60	Alcohol 600 " Water 300 "	400 "	900 "
Mezereum	" 30	Alcohol	400 "	900 "
Nux vomica	" 60	Alcohol 750 Cc. Water 250 " Acetic Acid 50 "	1050 "	
Pareira	" 40	Alcohol 720 " Glycerin 100 " Water 180 "	400 "	850 "
Phytolacca Root	" 60	Alcohol 600 " Water 300 "	400 "	800 "
Pilocarpus	" 40	Diluted Alcohol	350 "	850 "
Podophyllum	" 60	Alcohol 800 Cc. Water 200 "	300 "	850 "
Quassia	" 60	Alcohol 300 " Water 600 "	400 "	900 "
Rhamnus Purshiana	" 60	Diluted Alcohol	400 "	800 "
Rhubarb	" 30	Alcohol 800 Cc. Water 200 "	400 "	750 "
Rhus Glabra	" 40	Diluted Alcohol 900 " Glycerin 100 "	350 "	800 "
Rose	" 30	Diluted Alcohol 900 " Glycerin 100 "	400 "	750 "
Rubus	" 60	Alcohol 600 " Glycerin 100 " Water 300 "	350 "	700 "
Rumex	" 40	Diluted Alcohol	350 "	800 "
Sanguinaria	" 60	Alcohol 225 Cc. Water 75 " Acetic Acid 50 "	350 "	850 "
Sarsaparilla	" 30	Alcohol 300 " Water 600 "	400 "	800 "

Name.	Fineness of powder.	Initial Menstruum.	Quantity of Menstruum to moisten 1000 Gm. of the drug.	Reserve.
Fluid Extract of—				
Sarsaparilla, Compound	No. 30	Alcohol 300 Cc. Glycerin 100 " Water 600 "	400 Cc. 250 "	800 Cc. 900 "
Savin	" 40	Alcohol	350 "	850 "
Scoparius	" 60	Diluted Alcohol	350 "	800 "
Scutellaria	" 40	Diluted Alcohol		
Senega	" 40	Alcohol 750 Cc. Ammonia Water 50 " Water 200 "	450 " 400 "	850 " 800 "
Senna	" 30	Diluted Alcohol	300 "	900 "
Serpentaria	" 60	Alcohol 800 Cc. Water 200 "	200 "	750 "
Spigelia	" 60	Diluted Alcohol	300 "	850 "
Squill	" 20	Alcohol 750 Cc. Water 250 "	300 "	850 "
Stillingia	" 40	Diluted Alcohol	200 "	900 "
Stramonium Seed	" 60	Alcohol 750 Cc. Water 250 "	300 "	850 "
Taraxacum	" 30	Diluted Alcohol		
Triticum	Finely cut	Boiling Water		
Uva Ursi	No. 30	Alcohol 200 Cc. Glycerin 300 " Water 500 "	400 "	900 "
Valerian	" 60	Alcohol 750 Cc. Water 250 "	300 Cc.	850 "
Veratrum Viride	" 60	Alcohol	300 "	900 "
Viburnum Opulus	" 60	Alcohol 750 Cc. Water 250 "	300 "	850 "
Viburnum Prunifolium	" 60	Alcohol 750 " Water 250 "	300 "	850 "
Wild Cherry	" 20	Glycerin 100 " Water 200 " followed by a mixt. of Alcohol 850 Cc. Water 150 "	300 "	800 "
Xanthoxylum	" 40	Alcohol	250 "	900 "

Special Remarks.

Extractum Castaneæ Fluidum. The exhaustion of chestnut leaves, by percolation with cold water, is a tedious operation and necessitates subsequent prolonged evaporation. If the leaves be strongly expressed after maceration with hot water, and this treatment be repeated once or twice, with half the quantity of fluid, the extraction of the active virtues of the drug will be complete. The addition of a considerable quantity of alcohol to the concentrated infusion causes the precipitation of mucilaginous and albuminous matter, which is removed, and the filtered liquid, after evaporation to a definite volume, is preserved by the addition of glycerin and a further quantity of alcohol.

Extractum Glycyrrhizæ Fluidum. Liquorice root contains a sweet principle, glycyrrhizin, both in the free state and combined with ammonia, the former being insoluble but the latter soluble in cold water; the addition of ammonia-water to the menstruum is for the purpose of uniting ammonia with the free glycyrrhizin, and thus insuring the solution of the total sweet principle present. If liquorice

root which has been deprived of the brown corky layer be used, the flavor of the fluid extract will be far more agreeable.

Extractum Lupulini Fluidum. Lupulin is very rich in resin, which it yields readily to alcohol, and if the drug be moistened with one-fifth of its weight of menstruum, and then firmly packed as directed in the Pharmacopœia, the mass will become almost impermeable to the menstruum subsequently added; it is therefore better to pack the lupulin without previous moistening, which insures more satisfactory percolation.

Extractum Nucis Vomicæ Fluidum. There appears to be little necessity for this preparation alongside of the powdered extract and the tincture. The official directions, to digest the finely powdered drug for forty-eight hours, in a tightly-stoppered vessel, with a mixture of alcohol, water, and acetic acid, are important, and without this preliminary treatment complete exhaustion is very difficult, as the active principles are tenaciously imbedded in the horny albuminous matter of the seed, which latter is softened by the acetic acid and heat. The entire percolate is reduced to a definite weight, and after determining the amount of alkaloids present, the residue is dissolved in alcohol and so much of a mixture of alcohol and water added that each Cc. of the finished product shall contain 0.015 Gm. of alkaloids, which makes the fluid extract five times as strong as the tincture of nux vomica. The volume of fluid extract obtainable from a soft extract of known alkaloidal strength can be easily calculated; thus, if the extract contains exactly 1.5 per cent. of alkaloid, each gramme of extract, containing 0.015 Gm. of alkaloid, will yield 1 cubic centimeter of fluid extract; but if it contains more than 1.5 per cent., then each gramme will yield as many cubic centimeters as 1.5 is contained times in the number expressing the percentage. For instance, should the extract contain 12.5 per cent. of alkaloids, each gramme will yield 8.33+ Cc. of fluid extract; for $12.5 \div 1.5 = 8.33+$. Proof: 1.0 Gm. at 12.5 per cent. = 0.125 Gm., and 0.125 Gm. ÷ 8.33+ = 0.015 Gm., the amount of alkaloid required by the Pharmacopœia, in each Cc.

Extractum Rhamni Purshianæ Fluidum. The official formula yields an efficient but intensely bitter preparation. Bark which has been stored at least two years should be used, so as to overcome the tendency to griping and other unpleasant effects. The so-called tasteless fluid extract of cascara is usually prepared with the aid of calcined magnesia, of which from 100 to 125 Gm. are mixed with 1000 Gm. of the powdered bark and made into a soft paste with water; after standing for twelve hours this is dried, again powdered, and percolated with diluted alcohol, as in the official extract.

Extractum Pruni Virginianæ Fluidum. The formula for this fluid extract has been repeatedly changed with the view of insuring greater stability. A No. 30 powder of the bark seems better adapted for firm packing than No. 20, and the Pharmacopœia orders an unnecessarily strong alcoholic menstruum, the finished product containing

60 per cent. of alcohol. A menstruum composed of alcohol 2 volumes, glycerin 2 volumes, and water 6 volumes, has been found to yield a very satisfactory preparation, which precipitates but slightly, mixes clear with syrup, and retains the odor of hydrocyanic acid for a long time. Repercolation is best adapted for this fluid extract, since its value depends chiefly upon the volatile hydrocyanic acid, which is generated during the maceration and percolation of the drug.

Extractum Rhei Fluidum. The very large proportion of alcohol directed in the official formula has been found necessary after a series of experiments with various mixtures of alcohol and water, both with and without the addition of glycerin. The present fluid extract precipitates only very slightly, and retains its original fluidity for several years, but does not form clear mixtures with aqueous or saccharine liquids unless an alkali be added.

Extractum Sanguinariæ Fluidum. This fluid extract formerly caused much annoyance by copious precipitation on the bottom and sides of the containers. The presence of 5 per cent. of acetic acid and a less alcoholic menstruum have been found to improve the character of the preparation, but precipitation can probably never be entirely prevented.

Extractum Sarsaparillæ Fluidum. Since glycerin has been dropped from the official menstruum, a slight increase in the alcoholic strength appears desirable, and although water alone is capable of extracting the virtues of sarsaparilla, a mixture of 2 volumes of alcohol and 3 volumes of water will yield a better and more stable preparation.

Extractum Scillæ Fluidum. A strongly alcoholic menstruum is desirable for squill, as the drug contains much gummy and albuminous matter, which would affect the stability of the fluid extract.

Extractum Scutellariæ Fluidum. When made with diluted alcohol this fluid extract does not keep so well as when made with 2 volumes of alcohol and 1 volume of water; hence the latter mixture is to be preferred.

Extractum Senegæ Fluidum. Ammonia water is used in the menstruum, to form soluble compounds with the pectin principles present in the drug, and thus prevent gelatinization of the fluid extract. The active virtues of senega are far more soluble in water than in alcohol, but the former also extracts larger proportions of pectin compounds, and these must be avoided as far as possible. A menstruum composed of 2 volumes of alcohol and 1 volume of water, with the addition of 5 per cent. of ammonia water, exhausts the drug thoroughly and yields a permanent preparation, hence the stronger alcoholic menstruum ordered by the Pharmacopœia is unnecessary.

Extractum Stillingiæ Fluidum. This fluid extract will sometimes gelatinize on standing; this may be avoided either by using a stronger alcoholic menstruum (alcohol 3 volumes, water 1 volume), or, what is still better, by adding sugar in the proportion of 10 or 12 per cent. of the weight of the drug.

[illegible] *Tritici Fluidum.* Although the Pharmacopœia directs [illegible] with boiling water to exhaustion, digestion of the finely-[illegible] will be found preferable in every way, the operation to be [illegible] once or twice as may be necessary; the infusion should then [illegible] concentrated, and when cold mixed with alcohol and set [illegible] two days, whereby the mucilaginous and albuminous matter [illegible]. The finished product contains 25 per cent. of alcohol, [illegible] the saccharine liquid against fermentation.

[illegible] *Uvæ Ursi Fluidum.* The large quantity of glycerin, 30 [illegible] contained in the official fluid extract, is probably necessary [illegible] with the very weak alcoholic menstruum ordered, but [illegible] on keeping equally well can be made by using diluted [illegible] and omitting the glycerin entirely.

[illegible] *Veratri Viridis Fluidum.* There seems to be little or no [illegible] for this preparation, as the drug is well represented by the [illegible] If carefully made, the fluid extract is two and a half times [illegible] as the tincture, and presents all the alkaloids and resins of [illegible] in the form of a concentrated solution.

CHAPTER XXIII.

EXTRACTS.

EXTRACTS are permanent, soft, solid, or dry preparations, obtained by evaporation of a solution of the medicinal principles of drugs. These solutions are prepared, as a rule, in the manner already explained under fluid extracts, the solvents or menstrua employed being either water, water and alcohol, alcohol, or ether, according to the different menstrua used in their manufacture. Extracts are divided into *aqueous*, *hydro-alcoholic*, *alcoholic*, and *ethereal*, the last-named class being recognized in the Pharmacopœia under the name of *oleoresins*. In fresh plants, the solution of the medicinal principles is represented by the juice, and may be obtained by expression; extracts prepared by simple evaporation of the fresh juice of a plant are usually known as inspissated juices.

Our Pharmacopœia recognizes but one extract made from the fresh plant, extract of taraxacum, since the narcotic herbs which are extensively used in Europe for this purpose are not indigenous to this country. The juice is obtained from the fresh plant, after removal of extraneous matter, by bruising in a stone mortar with the aid of a hard-wood pestle until reduced to a smooth pulpy mass, which is then strongly expressed in canvas bags; in order to recover all the juice, the residue is often mixed with water and again expressed. When the plant is not sufficiently moist to enable the formation of a soft pulp, water is sprinkled over it from time to time, as directed in the Pharmacopœia.

Besides the medicinal principles, the expressed juices of fresh herbs contain also mucilaginous and albuminous matter in solution and variable quantities of chlorophyll or green coloring matter in suspension; of these the albuminous principles are most objectionable, as upon concentration of the juice they undergo change and are apt to render the finished extract tough and insoluble. When roots are expressed, as in the case of the corm of colchicum, starch, which is present in the juice in place of chlorophyll, passes through the press-cloth, and must be removed by subsidence and decantation. The British, German, and French Pharmacopœias direct the removal of albuminous matter by heating the juice to from 80° to 90° C. (176° to 194° F.) and filtering. The coagulated albumen envelops the green coloring matter and removes it also, which fact is disregarded in Germany and France, and accounts for the brown color of the extracts made from fresh herbs in those countries. In Great Britain the chlorophyll is carefully separated by heating the fresh juice to

lation, a menstruum uniform in alcoholic strength being employed during the process of exhaustion. When, however, glycerin is used with the first portion of the menstruum, percolation is continued and finished with a liquid of the same alcoholic strength, but not mixed with glycerin; the only exception to this is in the case of fluid extract of wild cherry, where the drug is moistened and packed with a mixture of glycerin and water, and then percolated with alcohol and water. With the exception of castanea and triticum, a certain portion of the stronger percolate is set aside as a reserve, and the weaker percolate is directed to be evaporated to a soft extract, which is dissolved in the reserved portion, the requisite volume of finished product being made up with fresh menstruum containing no glycerin. By evaporating the weak percolate to a soft extract, most of the water is also expelled, and the comparatively small portion remaining with the extract will occasion but a slight change in the menstruum of the reserved portion, which, at the same time, is the best solvent for the extractive matter; finally, the addition of fresh menstruum will not change the alcoholic strength of the liquid.

It is important that the exhaustion of the drug be conducted as carefully as possible, so that the reserved portion may represent a solution of nearly the whole active virtues of the drug; with this end in view the rate of percolation for 1000 Gm. of drug should be adjusted to about 8 drops per minute, at which rate about 20 Cc. can be collected in an hour. In the hands of a careful operator handling such quantities as are given in the pharmacopœial formulas, the official process yields very satisfactory results, and the danger arising from evaporation of the weak percolate may well be disregarded, since from 90 to 95 per cent. of the active principles are most likely contained in the reserved portion, therefore, only a trifling proportion of the medicinal virtues of the drug will be subjected to heat.

The official directions for the preparation of fluid extracts are intended for the quantity of drug designated in the formulas, and must of necessity often be modified by manufacturers who operate upon hundreds of pounds at one time; fineness of powder, degree of packing and rate of percolation must be adapted to the quantity of material in hand. Manufacturers, in some cases, resort to repeated maceration and expression instead of percolation.

Special authority is given by the Pharmacopœia to employ, where it may be applicable, the process of repercolation without change of initial menstruum. This process, which is fully described on page 130, is followed by several manufacturers, and does away with the possibility of injury from application of heat. Repercolation is particularly adapted to the preparation of fluid extracts, and the only objection that can be urged against its use is the enforced necessity of carrying on hand a series of bottles containing weak percolates, for each fluid extract made; disregarding this annoying feature, the process is less troublesome than any other, and in the case of some drugs must yield fluid extracts of superior quality.

It is not known whether the so-called *colorless extractive* is alike in all plants, neither is its composition or the nature of the changes produced under the conditions mentioned known, except that the heat of boiling water and the prolonged action of oxygen will convert it ultimately into a blackish insoluble substance, to which the name *apotheme* has been given, and which appears to be allied to *humin*. Extractive is almost insoluble in absolute alcohol and ether, but dissolves freely in weaker alcohol and water, and is removed from its solution by animal charcoal and aluminum hydroxide, the more readily after it has become colored by oxidation. It is with difficulty freed from all admixtures, and the terms sweet, bitter, acrid, etc., as applied to extractives, refer to the same body in a more or less altered condition, combined or intimately mixed with other principles to which the peculiar taste is due. The injurious influence of air and heat upon the vegetable juices is mainly confined to the alterations of this extractive, and extends, in a limited degree only, to the majority of the well-defined principles. Its effects have often been much overrated, except as regards the appearance of the extracts. The color of the different extracts varies with the nature of the drug from which they have been made, but should never be black. The characteristic taste, and to some extent also the odor of the drug, should be perceived in the extracts, and these should yield a nearly clear or moderately turbid solution with the menstruum used in their preparation.

Aqueous Extracts. While decoction in some cases increases the yield of extract, by bringing into solution starch and other inert matter, it more frequently injures the quality of the product, by inducing changes in certain principles, which do not occur by infusion at lower temperatures. There is but one instance, that of extract of logwood, in which the Pharmacopœia directs extraction by boiling, and this is on account of the difficulty of exhausting the tough wood. In Europe, digestion is still preferred for a few aqueous extracts, but, as a rule, maceration and percolation with cold water have been found to yield superior extracts. For the better extraction of the active virtues of the drug, an addition of acid or alkali is sometimes made, as in the case of the official extracts of colchicum root and pure extract of glycyrrhiza. In the preparation of aqueous extracts the solution is freed from objectionable matter, whenever necessary, by heating to the boiling-point and straining before final evaporation.

In 1889, the plan of concentrating large volumes of aqueous solutions of extracts by means of cold was formulated by M. Adrian, a French pharmacist, and put into practice on a large scale. Following up the suggestions of Herrera (1877), M. Adrian subjects the filtered aqueous solutions to a temperature of —20° C. (—4° F.), in an ammonia-ice apparatus, and thus obtains large blocks of ice, in which the extractive solution is enveloped, the pure water alone freezing; these blocks of ice are rapidly converted into snow, by means of

alcohol alone, two with alcohol and glycerin, twenty-one with diluted alcohol, forty-six with various mixtures of alcohol and water, or alcohol, water, and glycerin, and in two, water only is used as a menstruum, although the preparation is finally preserved with alcohol; altogether, sixteen contain glycerin. In the case of four drugs, conium, ergot, nux vomica, and sanguinaria, acetic acid is added to the initial menstruum, to facilitate the extraction of the alkaloidal principles present; in the case of senega and of glycyrrhiza, ammonia water is added to the solvent, to prevent gelatinization in the former fluid extract, and to insure complete solution of the sweet principle in the latter drug. Arranged according to the menstruum, the official fluid extracts may be divided into twenty-one classes, as follows:

17 Made with alcohol: Aromatic powder, buchu, calamus, cannabis indica, capsicum, cimicifuga, cubeb, gelsemium, ginger, grindelia, iris, kusso, lupulin, mezereum, savin, veratrum viride, xanthoxylum.

1 Made with alcohol 4 volumes, glycerin 1 volume: Cinchona.

1 Made with alcohol 3 volumes, glycerin 1 volume: Cotton-root bark.

5 Made with alcohol 4 volumes, water 1 volume: Belladonna root, eriodictyon, podophyllum, rhubarb, serpentaria.

15 Made with alcohol 3 volumes, water 1 volume: Aconite, arnica root, black-haw, calumba, eucalyptus, guarana, ipecac, leptandra, matico, squill, stramonium seed, valerian, viburnum opulus. Same menstruum with addition of acetic acid: Nux vomica, sanguinaria.

8 Made with alcohol 2 volumes, water 1 volume: Bitter orange peel, chirata, colchicum root, colchicum seed, digitalis, hyoscyamus, menispermum, phytolacca root.

20 Made with diluted alcohol: Asclepias, chimaphila, coca, convallaria, cypripedium, dulcamara, eupatorium, gentian, lappa, lobelia, pilocarpus, rhamnus purshiana, rumex, scoparius, scutellaria, senna, spigelia, stillingia, taraxacum. Same menstruum with addition of acetic acid: Conium, ergot.

8 Made with alcohol 5 volumes, water 8 volumes: Frangula.

Made with alcohol 1 volume, water 2 volumes: Quassia, sarsaparilla.

1 Made with alcohol 72 volumes, water 18 volumes, glycerin 10 volumes: Pareira.

1 Made with alcohol 65 volumes, water 25 volumes, glycerin 10 volumes: Apocynum.

3 Made with alcohol 6 volumes, water 3 volumes, glycerin 1 volume: Aspidosperma, hydrastis, rubus.

4 Made with diluted alcohol 9 volumes, glycerin 1 volume: Geranium, krameria, rhus glabra, red rose.

1 Made with alcohol 5 volumes, water 8 volumes, glycerin, 1 volume: Hamamelis.

1 Made with alcohol 3 volumes, water 6 volumes, glycerin 1 volume: Sarsaparilla (compound fluid extract).

/ Made with alcohol 2 volumes, water 5 volumes, glycerin 3 volumes: Uva ursi.

/ Made with alcohol 75 volumes, water 20 volumes, ammonia water 5 volumes: Senega.

/ Made with alcohol 30 volumes, water 65 volumes, ammonia water 5 volumes: Glycyrrhiza.

/ Made with water 2 volumes, glycerin 1 volume, followed by a mixture of alcohol 85 volumes, water 15 volumes: Wild cherry.

/ Made with boiling water: Triticum. The finished product contains about 25 per cent. by volume of alcohol.

/ Made with boiling water and cold water: Castanea. The finished product contains 10 per cent. by volume of glycerin and about 20 per cent. by volume of alcohol.

Alphabetical List of Official Fluid Extracts,

Showing the fineness of powder, menstruum, degree of moisture, and reserve percolate directed by the Pharmacopœia.

Name.	Fineness of powder.	Initial Menstruum.	Quantity of Menstruum to moisten 1000 Gm. of the drug.	Reserve.
Fluid Extract of—				
Aconite	No. 60	Alcohol 750 Cc. Water 250 "	400 Cc.	900 Cc.
Apocynum	" 60	Alcohol 650 " Glycerin 100 " Water 250 "	400 "	900 "
Arnica Root	" 60	Alcohol 750 " Water 250 "	400 "	900 "
Aromatic Powder	.....	Alcohol	350 "	850 "
Asclepias	No. 60	Diluted Alcohol	400 "	900 "
Aspidosperma	" 60	Alcohol 600 Cc. Glycerin 100 " Water 300 "	400 "	800 "
Belladonna Root	" 60	Alcohol 800 " Water 200 "	350 "	900 "
Bitter Orange Peel	" 40	Alcohol 600 " Water 300 "	350 "	800 "
Buchu	" 60	Alcohol	400 "	850 "
Calamus	" 60	Alcohol	350 "	900 "
Calumba	" 20	Alcohol 750 Cc. Water 250 "	300 "	700 "
Cannabis Indica	" 20	Alcohol	300 "	900 "
Capsicum	" 60	Alcohol	500 "	900 "
Castanea	" 30	Boiling Water followed by Cold Water		
Chimaphila	" 30	Diluted Alcohol	400 "	700 "
Chirata	" 30	Alcohol 600 Cc. Water 300 "	350 "	850 "
Cimicifuga	" 60	Alcohol	250 "	900 "
Cinchona	" 60	Alcohol 800 Cc. Glycerin 200 "	350 "	750 "
Coca	" 40	Diluted Alcohol	450 "	800 "
Colchicum Root	" 60	Alcohol 600 Cc. Water 300 "	350 "	850 "
Colchicum Seed	" 30	Alcohol 600 " Water 300 "	300 "	850 "
Conium	" 40	Diluted Alcohol 980 " Acetic Acid 200 "	300 "	900 "
Convallaria	" 60	Diluted Alcohol	400 "	800 "
Cotton Root Bark	" 30	Alcohol 750 Cc. Glycerin 250 "	500 "	700 "
Cubeb	" 60	Alcohol	400 "	900 "
Cypripedium	" 60	Diluted Alcohol	400 "	900 "
Digitalis	" 60	Alcohol 600 Cc. Water 300 "	400 "	850 "
Dulcamara	" 60	Diluted Alcohol	400 "	800 "

Fel Bovis Purificatum, U. S. P. Fresh ox-gall contains considerable mucilaginous matter which, upon concentration of the former, renders the inspissated mass tough and unmanageable; this can be removed with alcohol, and as liquid fresh bile is unfit for internal administration, purification is necessary. The Pharmacopœia directs that fresh ox-gall be evaporated on a water-bath to one-third its volume, and then mixed with an equal bulk of alcohol and set aside in a covered vessel for three or four days; the clear solution is then decanted, the remainder filtered, and the mixed liquids evaporated to a pilular consistence.

A simple test of the quality of purified ox-gall is to dissolve it in water, when a clear solution should result which should remain transparent upon addition of an equal volume of alcohol.

The Official Extracts.

Of the thirty-two extracts recognized in the Pharmacopœia, six are made with alcohol, *Aconite, Indian Cannabis, Cimicifuga, Iris, Jalap, and Physostigma*; two are made with *a mixture of* alcohol 4 volumes and water 1 volume, *Podophyllum, and Rhubarb*; three are made with *a mixture of* alcohol 3 volumes and water 1 volume, *Cinchona, Leptandra and Nux Vomica* (*with addition of acetic acid*); four are made with *a mixture of* alcohol 2 volumes and water 1 volume, *Belladonna Leaves, Digitalis, Euonymus, and Hyoscyamus*; six are made with diluted alcohol, *Arnica Root, Colocynth, Conium* (*with addition of acetic acid*), *Ergot* (*with addition of acetic acid*), *Stramonium Seed, and Juglans*; one is made with *a mixture of* alcohol 2 volumes and water 5 volumes, *Uva Ursi*; eight are made with water, *Aloes, Colchicum Root* (*with addition of acetic acid*), *Gentian, Glycyrrhiza* (*with addition of ammonia water*), *Hæmatoxylon, Krameria, Opium, and Quassia*; one is an inspissated juice, *Taraxacum*; one, called a compound extract, is made by mixing the several ingredients together and then powdering the mixture, *Compound Extract of Colocynth.*

Alphabetical List of Official Extracts,

Showing the fineness of the powdered drug, the menstruum used, the required moisture, and the average yield.

Name.	Fineness of Powder.	Menstruum.	Quantity of menstruum to moisten 1000 Gm. of the drug.	Degree of Packing.	Reserve.	Average. Yield.
Extractum—						
Aconiti . . .	No. 60	Alcohol	400 Cc.	Firm	900 Cc.	20 per ct.
Aloes	.....	Boiling Water	.....	.....	.....	50 "
Arnicæ Radicis	" 60	Diluted Alcohol	400 "	Firm	900 Cc	25 "
Belladonnæ Foliorum Alcoholicum	" 60	Alcohol 2 vols. Water 1 "	400 "	"	900 "	20 "
Cannabis Indicæ	" 20	Alcohol	300 "	"	.....	12½ "
Cimicifugæ . .	" 60	Alcohol	250 "	"	.....	15 "
Cinchonæ . .	" 60	Alcohol 750 Cc. Water 250 " followed by diluted alcohol	350 "	"	.....	20 "
Colchici Radicis	" 60	Acetic Acid 350 Cc. Diluted Alcohol 1500 " followed by Water	500 "	Moderate	.....	22 "
Colocynthidis .	" 20	Diluted Alcohol	.....	.....	From pulp 40 " From pulp & seed 15 "	
Colocynthidis Compositum	This Extract is a mixture of 160 parts Extract of Colocynth, 500 parts of Purified Aloes, 140 parts each of Resin of Scammony and Soap and 60 parts of Cardamom.					
Conii	No. 40	Acetic Acid 20 Cc. Diluted Alcohol 980 "	300 Cc.	Firm	900 Cc	20 per ct.
Digitalis . . .	" 60	Alcohol 2 vols. Water 1 vol.	400 "	"	.....	25 "
Ergotæ . . .	" 60	Acetic Acid 20 Cc. Diluted Alcohol 980 " Extract of Ergot is officially directed to be made by simple evaporation of the fluid extract	300 "	"	850 Cc.	15 "
Euonymi . .	No. 30	Alcohol 2 vols. Water 1 vol.	400 Cc	Firm	.....	20 per ct.
Gentianæ .	" 20	Water	400 "	.....	.....	33 "
Glycyrrhizæ Purum	" 20	Ammonia Water 150 Cc. Water 1000 "	1000 "	Moderate	.....	20 "
Hæmatoxyli .	Rasped	Water	....	.....	.....	10 "
Hyoscyami . .	No. 60	Alcohol 2000 Cc. Water 1000 " followed by diluted alcohol	400 "	Firm	900 Cc.	24 "
Iridis	" 60	Alcohol	400 "	"	.....	16 "
Jalapæ . . .	" 60	Alcohol	350 "	"	900 Cc	18 "
Juglandis . .	" 30	Diluted Alcohol	400 "	"	.....	15 "
Krameriæ . .	" 40	Water	300 "	.....	.....	12 "
Leptandræ . .	" 40	Alcohol 3 vols. Water 1 vol.	400 "	Firm	.....	12 "
Nucis Vomicæ .	" 60	Acetic Acid 50 Cc. Alcohol 750 " Water 250 "	1000 "			
Opii . . .	Very fine powder	Water				
Physostigmatis	No. 80	Alcohol	400 "	Firm	900 Cc.	6 per ct.
Podophylli . .	" 60	Alcohol 4 vols Water 1 vol.	300 "	"	.....	20 "
Quassiæ . . .	" 20	Water	400 "	"	.....	4 "
Rhei	" 30	Alcohol 4 vols. Water 1 vol.	400 "	"	1000 Cc.	25 "
Stramonii Semin.	" 60	Diluted Alcohol	300 "	"	900 Cc	7 "
Taraxaci . . .	.....	The official extract is an inspissated juice.			.....	10 "
Uvæ Ursi . .	No. 30	Alcohol 2 vols. Water 5 "	400 Cc.	"	900 Cc.	25 "

Special Remarks.

Extractum Aconiti. If carefully prepared, this extract represents all the active principles of aconite root, in a very concentrated form; it is about five times as powerful as the root itself or the fluid extract, and should not be confounded with the extract of aconite of the British Pharmacopœia, which is the inspissated juice of fresh aconite leaves, and a much weaker preparation.

Extractum Aloes. Extract of aloes may be prepared from either Barbadoes or Socotrine aloes, the latter variety being generally preferred in this country. The large proportion of water ordered by the Pharmacopœia is for the purpose of avoiding the admixture of resin; a concentrated aqueous solution of aloes retains in solution the resin present, whereas a dilute solution again deposits it on cooling. The extract does not yield a perfectly clear solution with water, as complete separation of resinous matter is impossible. The extract, when properly made, is brittle and is easily converted into a yellow brown powder.

Extractum Belladonnæ Foliorum Alcoholicum. This extract is of a deep brownish-green color and possesses a heavy narcotic odor. It is admirably adapted for incorporation in ointments and plasters, for which purpose it is usually softened with a few drops of water. The full official title of the extract is never used by physicians, the more familiar term *Extractum Belladonnæ* being employed in prescription writing. In Great Britain, the name *Extractum Belladonnæ* refers to the inspissated juice of fresh belladonna herb, and the name *Extractum Belladonnæ Alcoholicum* is applied to an alcoholic extract of belladonna root, a preparation more powerful than our own official extract; these differences must be borne in mind when compounding British prescriptions and other formulas.

Extractum Cannabis Indicæ. Extract of Indian hemp is not of uniform quality, owing to the variable character of the drug; it is of blackish-green color and has a peculiar rather unpleasant heavy odor. The drug is rich in resin, which, together with the alkaloids present, is extracted completely by alcohol; the extract is soluble also in ether, chloroform, oil of turpentine and fixed oils. Its alcoholic solution is precipitated by solution of potassa or soda, the resin being insoluble in alkalies.

Extractum Cinchonæ. With a little care, cinchona can be completely deprived of its alkaloids by percolation with the official menstruum; the extract, which is of a reddish-brown color, is apt to become tough in the course of time, and should be incorporated with 10 per cent. of its weight of glycerin. The Pharmacopœia makes no requirements as to alkaloidal strength, but, if made from choice bark, the extract may contain as much as 25 or 30 per cent. of total alkaloids, being from five to six times as strong as the drug itself.

Extractum Colchici Radicis. The menstruum directed for this extract is of about the same strength as diluted acetic acid; the extract,

which is of brown color and bitter taste, is of a soft consistence, and cannot be rolled into pills by itself. The British extract and acetic extract of colchicum are both made from the fresh corm, in which condition it is said to be more active.

Extractum Colocynthidis. In order to avoid the fixed oil which is present in the seeds, the Pharmacopœia directs that only the pulp of the colocynth shall be used; maceration and expression are preferred to percolation, on account of the spongy character of the material. The yield of extract varies from 40 to 50 per cent. if made from good pulp; if calculated for the well-dried whole fruit, it ranges from 14 to 20 per cent. Many manufacturers allow the seeds to remain in the fruit, being careful not to have them crushed during the grinding. The presence of fixed oil in the extract would prevent evaporation to dryness and subsequent reduction to powder.

Extractum Colocynthidis Compositum. Since a perfectly homogeneous preparation cannot be obtained by simply mixing the ingredients in fine powder, the Pharmacopœia very properly directs that an intimate mixture shall be effected with the aid of heat and alcohol; when the alcohol has again been evaporated and the mass becomes brittle, the powdered cardamom is incorporated, and the vessel covered until cold, so as to avoid loss of volatile oil. The dry compound extract is finally reduced to powder. It contains half its weight of purified aloes, 16 per cent. of dry extract of colocynth, 14 per cent. each of soap and resin of scammony, and 6 per cent. of cardamom.

Extractum Conii. This extract can be conveniently prepared by carefully evaporating the official fluid extract, in a porcelain dish, at a low temperature; it is about five times as strong as the latter preparation. The herb and root of conium possess only very slight medicinal virtue, which latter resides in the volatile alkaloid *coniine.* Extractum Conii of the British Pharmacopœia is the inspissated juice of fresh conium leaves and branches, and a much feebler preparation than our extract. Good extract of conium, when triturated with solution of potassa or lime-water, should evolve the disagreeable characteristic odor of coniine, in a marked degree resembling that of mice.

Extractum Ergotæ. Extract of ergot, prepared by evaporating the fluid extract, represents the crude drug in the proportion of about 1 to 6, the yield from 150 Cc. of fluid extract being about 24 Gm. It is sometimes dispensed, under the name of ergotin, in the form of pills and suppositories. Several of the European pharmacopœias apply the name *ergotin* to a purified extract of ergot prepared by evaporating an aqueous infusion of ergot to a syrupy consistence and mixing with alcohol, whereby certain constituents (scleromucin and others) are precipitated; after filtration the clear liquid is evaporated to a soft consistence. This was essentially the method of Bonjean, who first applied the name *ergotin* to the extract of ergot made by himself in 1842.

The new Swiss Pharmacopœia (1893), on the strength of the results following the investigations of Kobert and Keller, which prove that the medicinal virtues of ergot reside in the alkaloid cornutine, has adopted the following formula for preparing extract of ergot for hypodermic use. 1000 Gm. of powdered (No. 40) ergot are exhausted by percolation with 70 per cent. (by volume) alcohol; the percolate is evaporated to 250 Gm., mixed with an equal weight of water and filtered when cold. The residue is well washed with water and the liquid likewise filtered. 50 Gm. of 10 per cent. hydrochloric acid are added to the mixed filtrates and the mixture set aside for twenty-four hours; after again filtering and washing the filter with water as long as the washings continue acid, 20 Gm. of crystallized sodium carbonate are gradually added. When the evolution of carbon dioxide has ceased, the liquid is evaporated to 150 Gm.; 15 Gm. of glycerin are then added, and the whole evaporated to 125 Gm. All the alkaloid is retained in solution, while much useless matter, fixed oil, resin, coloring matter, etc., are removed; a small amount of sodium chloride remains in the extract, but is not hurtful. The extract thus prepared is of the consistence of thick honey, and 1 Gm. represents 8 Gm. of ergot; it forms a reddish-yellow, perfectly clear solution with water.

Extractum Gentianæ. All of the valuable bitter principles of gentian are soluble in cold water, while much inert matter is avoided by the use of this menstruum; when hot water is employed the yield of extract is vastly increased on account of the large quantity of pectin compounds taken up. The object of boiling the cold water percolate, as directed in the U. S. Pharmacopœia, is to coagulate the albuminous matter, after removal of which the extract obtained forms an almost clear solution with water. To judge from the tough condition and imperfect solubility of many commercial extracts of gentian, manufacturers must frequently resort to heat in the exhaustion of the drug. With cold water, gentian yields about 30 per cent. of extract, which can be increased to 50 or 60 per cent. with hot water; the United States, German, French, and Swiss Pharmacopœias all direct cold water, but the British Pharmacopœia, strange to say, recommends boiling for fifteen minutes, followed by expression.

Extractum Glycyrrhizæ Purum. The official formula for this extract yields a preparation perfectly soluble in water, which is not the case with the ordinary extract of commerce, in mass or powder. The addition of ammonia water to the menstruum insures, as already explained under fluid extract of liquorice root, the complete extraction of the sweet principle, whilst the use of cold water prevents the solution of starch and much other inert matter. The yield of extract varies from 16 to 25 per cent.

Extractum Hæmatoxyli. The medicinal value of logwood lies in its astringent principle, which cannot be entirely extracted with cold water, hence boiling is officially directed. It is important that all contact with metal be avoided on account of the tannin, and the

extract should yield a clear, purplish-red solution with water. Extract of hæmatoxylon is well adapted for the dry condition, as it is non-hygroscopic; its taste is sweetish and afterward astringent. The commercial extracts of logwood sold in boxes are not fit for medicinal purposes, being only partly soluble in cold water.

Extractum Hyoscyami. The extracts of hyoscyamus of the British and German Pharmacopœias must not be confounded with that officially recognized in our Pharmacopœia; the former are the inspissated juice of the fresh flowering herb, more variable in quality than the hydro-alcoholic extract. Cubical crystals sometimes found in the British extracts of hyoscyamus and belladonna have, upon examination, proved to be potassium chloride.

Extractum Jalapæ Jalap owes its valuable properties entirely to the resin it contains; hence a purely alcoholic menstruum yields the most efficient extract. After jalap has been exhausted by alcohol, water will yet dissolve out a large proportion of extractive, which upon trial has been found perfectly inert. Jalap yields on an average about 18 per cent. of alcoholic extract, and subsequently about 30 per cent. of aqueous extract additional. The British Pharmacopœia directs the incorporation of the aqueous extract with the alcoholic extract first obtained; hence the British extract is a much weaker preparation than our own.

Extractum Krameriæ. Cold water is an excellent solvent for the particular tannin present in rhatany, upon which the astringency of the drug depends; hot water will yield a larger percentage of extract, but this will not form a complete solution with water, while the cold water extract is soluble, and with the addition of sugar forms a perfectly clear liquid. A very weak alcoholic menstruum is said also to furnish an increased yield of extract, but with results similar to those produced by hot water. Decided astringency and a perfectly clear solution with warm water and sugar, are indications of a well-prepared extract.

Extractum Nucis Vomicæ. The difficulties attending the perfect exhaustion of nux vomica have already been explained under the fluid extract. The seed contains considerable fixed oil, a portion of which is apt to be dissolved by the hydro-alcoholic menstruum; therefore, as the Pharmacopœia directs the extract to be reduced to powder, the removal of the fatty matter becomes necessary. This is effected, as directed in the official formula, by concentrating the percolate to about 15 per cent. of the weight of drug used and then washing repeatedly with ether as long as this removes anything. The ether is recovered by distillation and the fatty residue treated with boiling water and acetic acid, in order to recover any alkaloid which the oil may have carried with it. After the acid aqueous liquid has been added to the ether-washed residue, the whole is evaporated to a soft extract, cooled and weighed, after which the percentage of moisture and alkaloids is determined. From these data is calculated the quantity of sugar of milk which must be added to the soft extract, so that it

can be dried and reduced to a fine powder containing 15 per cent. of alkaloids.

Example: Suppose the soft extract contains 22 per cent. of moisture and 18.72 per cent. of alkaloids, how much sugar of milk must be added? Answer: Each gramme requires the addition of 0.468 Gm. of sugar of milk, or 100 parts require 46.8 parts.

Calculation: 1.0 Gm. less 0.220 (22 per cent. of 1) = 0.780 Gm., the amount of dry extract obtainable from 1.0 Gm. of soft extract. Since no alkaloids are lost in drying, the percentage is increased from 18.72 per cent. in the moist to 24 per cent. in the dry extract, for 0.780 : 0.1872 = 1.0 : 0.24.

The Pharmacopœia requiring only 15 per cent. of alkaloids in the dry extract, the 0.780 Gm. must be brought, by addition of sugar of milk, to a weight of which 0.1872 Gm. shall represent 15 per cent., or in other words, 0.780 Gm. are equal to $\frac{15}{24}$ of the final weight of official powdered extract obtainable from 1.0 Gm. of the soft extract. The unknown final weight may be represented by x, whose value may be ascertained by solving the equation $0.15 : 1.0 = 0.1872 : x$, or, if $0.780 = \frac{15}{24}$ of x, then $x = \frac{24}{15}$ of 0.780; in either case the value of x will be 1.248.

Finally, 1.248 Gm. — 0.780 = 0.468 Gm., the weight of sugar of milk to be added.

Extractum Opii. Opium is easily exhausted with cold water, but instead of triturating the mixture of opium and water occasionally during twelve hours, it is better to rub the opium into a smooth paste with water in a mortar, wash this carefully into a flask or bottle, add the remainder of the water, cork the flask or bottle, and shake vigorously every hour or two; agitation is more easily accomplished and is more beneficial to the extraction of the soluble principles. The magma on the filter should be slowly percolated with water until the liquid is nearly colorless and only faintly bitter. After concentration of the percolate to about twice the weight of opium used, the moisture and morphine present are determined, in order to ascertain the amount of sugar of milk which must be added to the syrupy extract, so that, upon complete drying, it shall yield a powder containing 18 per cent. of crystallized morphine.

Example: Suppose the thick syrupy liquid is found to contain 72 per cent. of moisture and 7 per cent. of crystallized morphine, how much sugar of milk must be added? Answer: Each gramme will require the addition of 0.110 Gm. of sugar of milk.

Calculation: 1.0 Gm. less 0.720 (72 per cent of 1) = 0.280 Gm., the amount of dry extract obtainable from 1.0 Gm. of the syrupy liquid. 0.07 Gm. (7 per cent. of 1) of crystallized morphine present in 1 Gm. of the syrupy liquid, are equal to 25 per cent. in 0.280 Gm. of dry extract, as shown by the equation 0.280 : 0.07 = 1.0 : 0.25.

The Pharmacopœia requiring only 18 per cent. of crystallized morphine in the dry extract, the 0.280 Gm. must be brought, by addition of milk sugar, to a weight of which 0.07 Gm. shall repre-

sent 18 per cent., or in other words, 0.280 Gm. is equal to $\frac{18}{25}$ of the final weight of official powdered extract obtainable from 1.0 Gm. of the syrupy liquid. The unknown final weight may be represented by x, whose value may be ascertained by solving the equation, $0.18 : 1.0 = 0.07 : x$, or if $0.280 = \frac{18}{25}$ of x, then $x = \frac{25}{18}$ of 0.280; in either case the value of x will be practically 0.390 (actually 0.389).

Finally 0.390 Gm. — 0.280 Gm. = 0.110 Gm., the weight of sugar of milk to be added.

Extractum Quassiæ. This extract is prepared exactly like extract of gentian, and all the comments made upon the latter extract apply equally to this preparation. As extract of quassia is not used to any great extent, and is liable to become tough when old, the addition of 10 per cent of glycerin to the extract, while still warm, is advisable.

Extractum Rhei. Extract of rhubarb presents the only instance, among the official extracts, in which the Pharmacopœia directs that the reserve percolate shall be concentrated by spontaneous evaporation; it is very questionable whether this plan is followed by manufacturers. It is well known that the medicinal virtues of rhubarb are modified and sometimes injured by a high heat, but there can scarcely be any objection to the recovery of the alcohol from the reserve tincture, at a temperature below 50° C. (122° F.). The menstruum being strongly alcoholic (76 per cent.), the alcohol is readily volatilized. During the final evaporation of the extract to the pilular consistence, it is important that stirring with a glass or porcelain rod be assiduously kept up, otherwise granular separation of resinous matter will occur.

Extractum Stramonii Seminis. The reduction of stramonium seed to No. 60 powder is difficult, on account of the large proportion of fixed oil present, which also renders the preparation of a satisfactory extract no easy task. If the seed be first freed from oil, by treatment with benzin, much better results will be obtained. Stramonium ointment made from the official extract does not possess the green color characteristic of the ointment made from an extract of the leaves.

Extractum Taraxaci. As already stated, the Pharmacopœia requires extract of taraxacum to be prepared from the fresh root; since the juice contains considerable albuminous matter which is not removed in the official process, the extract frequently becomes tough and imperfectly soluble. Much of the commercial extract of taraxacum is made from dried root, by percolation with water or a very weak alcoholic menstruum. True taraxacum root gathered in autumn is not always obtainable, and chicory root is frequently used as a substitute or as an adulterant.

Extractum Uvæ Ursi. Although the Pharmacopœia orders a mixture of 2 volumes of alcohol and 5 volumes of water as a menstruum for this extract, experience has shown that official diluted alcohol exhausts uva ursi completely and yields a more satisfactory preparation.

CHAPTER XXIV.

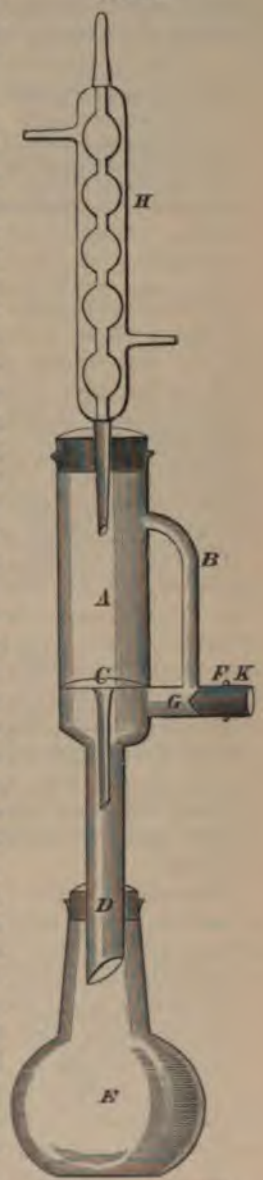
OLEORESINS AND RESINS.

Oleoresins.

SOLUTIONS of this class represent the medicinal virtues of the drugs from which they are made, in a more concentrated form than is possible in any other. They possess the power of self-preservation, and in this respect are superior to fluid extracts. Oleoresins consist chiefly of fixed or volatile oils associated with resin and other constituents; those officially recognized in the Pharmacopœia are all prepared by the same process, which consists in slowly percolating the drug in fine powder, with ether, to exhaustion, recovering the greater part of the ether by distillation, and finally removing the remaining ether by spontaneous evaporation. The percolation of drugs with ether requires the use of special apparatus (see page 121) to prevent loss of the very volatile solvent, and several attempts have been made to economize ether by using the same liquid over again until the material is exhausted, the best device for this purpose being the ether-extraction apparatus designed by Prof. Flückiger, illustrated in Fig. 203. The extractor, *A*, passes by means of the tube, *D*, through a cork into the receiving flask, *E*; at *C* is a septum or disk, upon which the material to be extracted is packed, and which communicates, by means of a small funnel-shaped tube, with *D*. The lateral tube, *B F*, passes into the tube, *G*, which is provided with a properly cut cork, *K*, so that the ether vapor may pass from the receiving bottle to a spiral condenser, *H*, fitted by means of a cork to the top of the extractor; the ether vapor can also be made to pass upward through the powder, by pushing the cork deeper into the tube, *G*, thus closing the orifice of the lateral tube, *B F*. A loose pledget of cotton is placed in the funnel tube at *C*, or a piece of filtering paper is placed over the small opening, to prevent the material from passing down. The whole apparatus may be made of any convenient size, of glass or tinned copper, and when in use the receiving flask is placed in warm water, for the purpose of vaporizing the ether, which is condensed above the extractor and drops back upon the powder, the process being continued until the material is exhausted. Another desirable feature of this apparatus is the recovery of the ether from the marc when the extraction of the drug has been completed. The lateral communication between *D* and *B F* is closed by means of the cork, and, applying a cold or wet sponge to the receiving flask, the ether vapor therein is condensed and a partial vacuum produced, which withdraws all the ether from the marc in the percolator above.

Experience has shown that when 2 Cc. of percolate have been obtained for each gramme of drug used, the latter will be practically exhausted, therefore percolation beyond this point is unnecessary; with the continuous extraction apparatus, half the quantity of ether can be made to accomplish the same results.

Fig. 203.



Fluckiger's Extraction Apparatus.

Considerable care is necessary in the recovery of ether by distillation, as official ether, which is directed to be used in the process, boils at about 37° C. (98.6° F.); the recovered ether should be but very slightly impregnated with the odor of volatile oil, and may be used again for a subsequent operation. Oleoresins are not used to any great extent at present, and are rarely made by the pharmacist himself; small quantities for use in prescriptions may be conveniently obtained by percolating some of the finely powdered drug in the barrel of a glass syringe and allowing the ether to evaporate in a warm place. The yield of oleoresin ranges from 5 to 60 per cent. for different drugs, and its consistence varies from liquid to a soft solid, dependent upon the amount of resin present.

On account of the volatile and inflammable character of ether, efforts have frequently been made to find a suitable substitute for the same; mixtures of ether and alcohol have been tried, as also petroleum benzin, but not with general satisfaction. The experiments of Mr. G. M. Beringer, in 1892, with pure acetone, have, however, conclusively proven the value of this solvent. Acetone is a product of the destructive distillation of calcium or barium acetate, and is now available in a very pure state; it is somewhat heavier than ether and boils at a point about 20° C. higher than that liquid. It is miscible in all proportions with water or alcohol, and possesses remarkable solvent properties. Drugs exhausted with acetone, when subsequently percolated with ether, have been found to yield nothing of value, and the oleoresins prepared with acetone are perfectly soluble in ether or alcohol and practically identical with those made with ether.

The Pharmacopœia recognizes six oleoresins prepared with ether, and, in every case, with one exception, the drug

is packed firmly into the percolator, previous moistening being quite unnecessary. On account of the large proportion of resin in lupulin, this drug must be packed lightly, otherwise the mass will become impacted. The following is an alphabetical list of the official oleoresins, showing the fineness of powder used and the average yield.

Name.	Fineness of Powder.	Average Yield.
Oleoresina Aspidii	No. 60	15 per cent.
Oleoresina Capsici	" 60	12 "
Oleoresina Cubebæ	" 30	22 "
Oleoresina Lupulini		60 "
Oleoresina Piperis	" 60	6.5 "
Oleoresina Zingiberis	" 60	6 "

Special Remarks.

Oleoresina Aspidii. This preparation is also known by the names *oleoresina filicis, extractum filicis æthereum,* and *oleum filicis maris.* As the root rapidly deteriorates upon keeping, only that having a fresh green color should be used. The oleoresin of male fern generally deposits, on standing, a granular crystalline substance largely composed of filicic acid, upon which depends the activity of the preparation, hence the necessity for thoroughly incorporating the deposit before dispensing the oleoresin. By percolation with acetone the drug has yielded as much as 18 per cent. of oleoresin.

Oleoresina Capsici. Owing to the large amount of fat present in capsicum, it is not desirable to carry percolation to complete exhaustion; experience, in fact, has taught that, if collected slowly, 150 Cc. of percolate will have practically exhausted 100 Gm. of the drug, and that further treatment simply loads the percolate with fatty matter. Oleoresin of capsicum is a dark, brownish-red liquid, which, shortly after being made, deposits granular fat; this is best removed by decanting the clear liquid and straining the residue, or washing the deposit rapidly with a little ether. Although the average yield of oleoresin has been reported as not over 5 or 6 per cent., from 12 to 16 per cent. of a very excellent preparation has frequently been obtained.

Oleoresina Cubebæ. Cubeb yields all its medicinal virtues to alcohol as well as ether; very satisfactory oleoresin has been made with the former menstruum. In Germany, the oleoresin is officially recognized under the name "*Extractum Cubebarum,*" and is prepared with a mixture of equal volumes of ether and alcohol. All oleoresin of cubeb deposits, upon standing, waxy matter and a crystalline body, cubebin, which, as the Pharmacopœia directs, should be rejected, only the liquid portion being dispensed. It is of a green or brownish-green color, and, when made with acetone, has been obtained to the extent of 25 per cent.

Oleoresina Lupulini. Lupulin is very rich in resin, hence a large yield of oleoresin is to be expected; it is of a reddish-brown color and has the consistence of a soft solid extract. While the average

yield is about 60 per cent., as much as 70 per cent. has been obtained with both ether and acetone, by complete exhaustion.

Oleoresina Piperis. Commercially this preparation is also known as *oil of black pepper*, which latter, however, is usually obtained as a by-product in the manufacture of piperin. Oleoresin of pepper, when first made, deposits piperin in crystalline form, which is separated by straining, leaving a thick, very black liquid. The yield with ether or acetone rarely exceeds 6 per cent.

Oleoresina Zingiberis. When made from uncoated (Jamaica) ginger the yield of oleoresin is less than from coated ginger, and is also lighter in color, thinner, and of a more agreeable flavor. The name *piperoid* has sometimes been applied to this preparation. From coated ginger as much as 10 per cent. of oleoresin has been obtained, while from Jamaica ginger the yield rarely exceeds 6 per cent.

Resins.

Under the title *Resinæ* the Pharmacopœia recognizes five preparations, two of which, however, are simply residuary products obtained in the distillation of the volatile oil from natural oleoresins. For the remaining three an official process of manufacture is given, alcohol being used as a solvent in each case; the resin is obtained by pouring a concentrated alcoholic tincture of the respective drugs into cold water and subsequently washing the precipitate repeatedly with water.

ALPHABETICAL LIST OF THE OFFICIAL RESINS.

Official Name.	How obtained.
Resina	Residue left after distillation of the volatile oil from Turpentine.
Resina Copaibæ	Residue left after distillation of the volatile oil from Copaiba.
Resina Jalapæ	By pouring a concentrated alcoholic tincture of Jalap into cold water.
Resina Podophylli	By pouring a concentrated alcoholic tincture of Podophyllum into cold water acidulated with hydrochloric acid.
Resina Scammonii	By pouring a concentrated alcoholic tincture of Scammony into cold water.

Special Remarks.

Resina Jalapæ. The amount of resin in jalap root varies considerably, ranging from 8 to 18 per cent., and it is not always possible to find commercial jalap which meets the official requirement of *not less than* 12 *per cent.* Resin of jalap differs from the official extract of jalap, in being free from water-soluble matter, of which the latter preparation contains quite an appreciable quantity; hence the official direction, to wash the precipitated resin twice with water, should be repeated until the washings are colorless; the adhering water is removed by drying the resin with a gentle heat. Not more that 10 per cent. of the resin of jalap should be soluble in ether, nor more than 7 per cent. in chloroform. The presence of common resin may

be detected by solubility in oil of turpentine and by gelatinization upon cooling a solution made by digesting the suspected resin in 10 parts of ammonia water at 80° C. (176° F.). Since resin of jalap has a slightly acrid but not bitter taste, an adulteration with aloes may be suspected if a pronounced bitter taste is observed. If resin of jalap be moistened with alcohol and then with a solution of ferric chloride, a green color should not be developed, nor should a blue color be observed if the inner surface of a fresh potato paring be rubbed with the resin, otherwise guaiac is present. That portion of jalap resin insoluble in ether, when dissolved in caustic alkali solution, is not reprecipitated upon addition of an acid; this property distinguishes jalap resin from other resins except that of scammony, and from the latter it differs by its insolubility in ether and oil of turpentine. While resin of scammony might become accidentally mixed with jalap resin, it would never be added as an adulteration, since it is far more expensive.

Resin of jalap may be obtained free from color, by treatment with animal charcoal; the best plan is to mix the charcoal with the powdered jalap before percolation and also to pass the percolate through animal charcoal.

Resina Podophylli. The object of adding hydrochloric acid to the water, before adding the alcoholic solution, is simply to facilitate the separation of the resinous matter. The yield of resin of podophyllum rarely exceeds 4 or 5 per cent., and its color should be from grayish-white to yellowish-green, provided no heat higher than 35° C. (95° F.) is used in drying it. According to Prof. Lloyd, who has had large experience in the manufacture of this resin, the concentration of the alcoholic tincture should not be carried beyond a very thin syrup, the water into which it is poured should be ice-cold, and the washed resin should be dried *without* heat, by exposure to air, in a cold place. Alum water is sometimes used to effect precipitation of the resin, but it yields a yellow product of inferior quality. The solubility of resin of podophyllum in ether varies from 50 to 85 per cent., depending upon the mode of its preparation, the better quality being most soluble and also lighter in color; according to Prof. Power, boiling water will dissolve about 80 per cent. of the resin if the treatment with fresh portions of the water be continued as long as anything is removed, but deposits most of it again on cooling. Resin of podophyllum forms a yellow liquid with solution of soda or potassa, from which it is re-precipitated by acids.

The name *podophyllin* is extensively applied in commerce to the resin, but does not always represent the official article.

Resina Scammonii. The Pharmacopœia directs that this resin be prepared from the gum-resin scammony and not from the root direct, as in the two preceding resins; hence treatment of the powder with boiling alcohol is directed instead of percolation. The yield of resin of scammony depends upon the quality of the gum-resin, and may vary from 70 to 90 per cent., alcohol taking up

only about 2 per cent. of water-soluble matter, according to Prof. Markoe.

Resin of scammony is wholly soluble in ether and oil of turpentine, and is not precipitated by acids from its solution in caustic alkalies. It is very slowly acted upon by sulphuric acid, whereas common resin is immediately turned intensely red; the presence of the latter can thus be detected. The resin of scammony can be distinguished from the gum-resin by not yielding a green emulsion when triturated with water.

CHAPTER XXV.

COLLODIONS.

UNDER this head are recognized in the Pharmacopœia four solutions, the base of which is pyroxylin, or soluble gun-cotton (see Cellulose, Part III.), and the solvent, a mixture of alcohol and ether. Collodions are employed only for external medication, and owing to the very volatile character of the solvent, they rapidly form a skin-like covering, or pellicle, when applied, which is impervious to water. Where a strong contractile coating is desired, the plain collodion is preferred, otherwise a less constringent and more comfortable covering is obtained by the addition of castor oil and Canada turpentine, as in the case of the official flexible collodion. For the purpose of medication, any substance soluble in ether may be added, such as iodine, iodoform, extract of Indian cannabis, salicylic acid, croton oil, mercuric chloride, veratrine, atropine, resorcin, pyrogallol, etc. Since pyroxylin is insoluble in water, the addition of the latter to collodion would cause immediate precipitation, hence all substances soluble only in water or alcohol and water, such as extract of belladonna, morphine sulphate, etc., are excluded from admixture. Collodions should always be preserved in tightly cork-stoppered bottles, in a cool place, remote from fire, on account of the ether present; care should also be taken that no collodion be allowed to remain on the lip or in the neck of the bottle after pouring out the liquid, to avoid "fixing" of the cork as the menstruum evaporates.

Collodions are best dispensed in small, round-shouldered vials provided with a cork through which a camel-hair pencil has been passed and securely fastened; this avoids loss of material and drying of the collodion in the brush—a very annoying occurrence.

ALPHABETICAL LIST OF OFFICIAL COLLODIONS.

Official Name.	Composition.
Collodium	Pyroxylin, 3 Gm.; Ether, 75 Cc.; Alcohol, 25 Cc.
Collodium Cantharidatum	Chloroformic Extract of Cantharides (representing 60 Gm Cantharides), 15 Gm ; Flexible Collodion, 85 Gm.
Collodium Flexile	Castor Oil, 3 Gm.; Canada Turpentine, 5 Gm.; Collodion, 92 Gm.
Collodium Stypticum	Tannin, 20 Gm.; Alcohol, 5 Cc.; Ether, 25 Cc.; Collodion, sufficient to make 100 Cc.

Special Remarks.

Collodium. If the pyroxylin has been carefully prepared, it should be perfectly soluble in the official menstruum, although a slight sedi-

ment of dirt, etc., occurs after the solution has been set aside for a few hours; from this the liquid can be carefully poured off, as filtration is impracticable. Anthony's collodion cotton, specially prepared for photographers' use, I have always found very satisfactory.

Collodium Cantharidatum. The value of cantharidal collodion will depend upon the quality of the powdered cantharides used and the care with which they are exhausted. Since chloroform is a very volatile menstruum, percolation must be conducted in a special apparatus (see Oleoresins), to avoid loss; the liquid is easily recovered by distillation on a water-bath, as chloroform boils at about 60° C. (140° F.). The extract dissolves readily in flexible collodion, by agitation, the finished product representing 60 per cent. of its weight of powdered cantharides, which makes it nearly twice as strong as the official cerate of cantharides.

Collodium Flexile. The addition of Canada turpentine (Canada balsam or balsam of fir) and castor-oil lends to collodion the property of forming a flexible pellicle which, while serving as a perfect covering to the part affected, yet permits perfect freedom of motion.

Collodium Stypticum. Owing to the large proportion of tannin ordered in the formula for styptic collodion, it is necessary to use a small quantity of diluent, ether and alcohol, with which the tannin is thoroughly mixed before the final addition of collodion. Flexible collodion is not suitable in this case, as a constringent pellicle is desired. Any impurities from the tannin, may be removed by rapidly straining the solution through gauze previously moistened with a little ether and alcohol.

CHAPTER XXVI.

EMULSIONS.

THE term "emulsion" is applied to a more or less permanent homogeneous liquid mixture composed of fatty, ethereal, or resinous substances and water, the former being suspended in a minutely divided state, which gives rise to the peculiar opaque and milk-like appearance. Nature provides types of true emulsions, in the form of milk, the natural food of all young mammalia, and the milk-like juices of certain plants from which the official and other gum-resins are obtained.

Those prepared by pharmacists, may be conveniently divided into natural and artificial emulsions; to the former class belong those which are made from seed or gum-resins, by simple trituration with water, Nature having provided the necessary emulsifying agent in intimate association with the oil or resin. Artificial emulsions are such as require the addition of some foreign body, by means of which the suspension of the oil or resin is made possible; to this class belong the majority of the emulsions prepared at the dispensing counter. Fixed and volatile oils, as well as ether, chloroform, oleo-resins and resins, are suitable for exhibition in the form of emulsion, the suspension in water being accomplished by the aid of appropriate excipients, such as acacia, tragacanth, yelk of egg, casein, dextrin, Irish moss, gelatin, soap-bark, etc. Oil-yielding seeds and natural gum resins contain albuminous and mucilaginous matter, by means of which the oil and resin can be brought into perfect suspension in water, and such emulsions approach more closely in character and stability to cow's milk, which may be looked upon as the most perfect emulsion known. The theory of emulsification is as follows: The insoluble liquid or solid, in a state of minute division, is completely surrounded or enveloped by the vehicle consisting of water and excipient, and thus an opaque mixture is produced, from which, the particles cannot separate by mere force of cohesion; such a condition can be obtained to perfection only by choice of a proper excipient, and, for artificial emulsions, none better than acacia has yet been found. Stability of artificial emulsions, while primarily dependent upon the division of the insoluble liquid into minute globules, is also influenced, to some extent, by the density of the vehicle, thus sugar has been found to increase the suspending power of gum materially; to prevent fermentative changes likely to arise in all aqueous vegetable solutions, alcohol or glycerin is frequently added to emulsions, in the proportion of one or two fluidounces for every pint.

With the exception of those made of volatile oils or ethereal liquids, emulsions should always be made in a mortar, either of unglazed Wedgewood or hard porcelain, having a flat bottom, and, in the case of seed or gum-resin emulsions, one of deep shape provided with a hard-wood pestle is to be preferred, in order to avoid injury from the force often necessary in crushing and manipulating the material. For making gum-resin emulsions, the cleanest and best tears should be selected, as the commercial fine powders are unfit for this purpose, partly because they are inferior in quality, and partly because they have been so modified by drying that when triturated with water they simply form an ordinary mixture from which the powder separates rapidly on standing; this change is due to dehydration, whereby the natural association of gum and resin has been broken up and their intimate union destroyed. For seed emulsions, when no other proportions are specified, 1 part of seed is used to 10 parts of water, all dirt and dust being carefully removed, if necessary, by washing with cold water. In both cases the material is crushed into a coarse powder, and, after the addition of a small quantity of water, beaten into a perfectly smooth pasty mass; to this, the remainder of the water is then added in divided portions, triturating the mass thoroughly and keeping it well scraped down from the pestle and sides of the mortar, so that a uniform mixture may result, which is finally passed through a well-wetted strainer of loose flannel or cheese-cloth, to remove the inert woody fibre and possible impurities. In making emulsion of lycopodium, it becomes necessary to triturate the seed *dry, with some pressure*, in order to rupture the hard seed envelope; when the powder changes in color and becomes damp and adhesive from the oil, a little water is added, with which a smooth soft paste can be formed, to be further diluted by the addition of water as directed above. Emulsion of lycopodium *should never be strained*, and, if properly made, will show no particles floating on the surface; the insoluble matter which settles upon standing is readily reincorporated by agitation.

Oil emulsions, which are far more frequently used (at least in this country) than those made from seed or gum-resins, require more care in their preparation, as success depends not only on the manipulation, but also on the judicious choice of a proper excipient. As a general rule, it may be stated that acacia produces the whitest and most stable emulsions, because its perfect and ready solubility in water, enables the operator to divide the oil quickly into minute globules, which are at once surrounded by an envelope of the mucilaginous liquid and thus kept from coalescing. The oil globules of a well-made acacia emulsion, when compared with milk under a magnifying lens more closely resemble its fat globules than would be the case if made with other excipients. To insure success, it is essential that definite proportions of oil, gum, and water be used for making the primary emulsion, which can then be diluted with water as desired. *Not less than one-fourth nor more than one-half* as much acacia as oil

should be used, and *not less than one and a half times nor more than twice as much* water as acacia.) The mixing of oil, gum, and water should not be effected by the usual method of trituration, which involves pressure of the pestle against the material on the bottom and sides of the mortar, and consequent development of heat, but should be brought about by a rapid light rotary movement of the wrist, communicated to the pestle held loosely in the hand, as shown in Fig. 204; this motion partakes more of that of an egg-whip, and the oil is thus rapidly broken up into minute globules in the presence of a viscid solution.

FIG. 204.

As stated before, emulsions of fats and fixed oils are best made in a flat-bottomed mortar, three distinct methods being in use to effect the desired object: namely, a milk-like liquid, miscible with water without the separation of oil globules. By many pharmacists the method usually recommended in Great Britain is preferred; this consists in making a smooth thick mucilage of granulated acacia and water, and then adding the oil by degrees, stirring assiduously until each portion of oil is emulsified—lastly adding the water for dilution, in divided portions. The other two are sometimes called the "Continental" methods, from the fact that they are used almost exclusively in Continental Europe. They do not direct the previous solution of the gum in water, and adhere strictly to definite proportions. While the so-called "English" method yields very satisfactory results in the hands of those accustomed to it, I much prefer, for the inexperienced, either of the other two methods, my preference being based upon observation of many hundred cases in the hands of students working in the laboratories. I have never known of a single failure by a novice to make a perfect emulsion according to the following methods, provided of course that the directions as given were followed.

Place in a mortar one-fourth as much *finely powdered* acacia as the oil to be used (7.5 Gm. of acacia for 30 Cc. of oil, or ʒij for fʒj), then add the oil and triturate well together into a smooth mixture. Now add *all at once*, not gradually, twice as much water as the acacia which has been used (15 Cc. of water for 7.5 Gm. of acacia, or fʒiv for ʒij), and stir rapidly until a perfect emulsion has been formed, which is known by the appearance of a white pasty mass, free from oil particles, and a peculiar crackling noise as the pestle is drawn through the adhesive mixture. This primary emulsion should be well scraped down with a spatula from the pestle and sides

of the mortar, again stirred, and then the remainder of the water slowly added with constant stirring. Granulated acacia cannot be used in this method, as with so small a quantity of gum it is necessary that it dissolve almost immediately, which will not occur with the granulated variety.

The second of the so-called "Continental" methods directs increased proportions of acacia and water, by which means an equally perfect, and at the same time denser, primary emulsion is obtained. One-half as much granulated acacia as oil is used, and one and a half times as much water as gum, or one-half as much water as oil and gum together; thus, oil 30 Cc. or f℥j, granulated acacia 15 Gm. or ℥iv, and water 22.5 Cc. or f℥vi. Place the acacia in a dry mortar, add the oil and water, and stir briskly until a perfect emulsion results, which dilute with the remaining water, as in the preceding method.

If from any cause the primary emulsion should fail, it will prove a loss of time and labor to endeavor to save it by addition of gum or water, provided the right proportions were used in the first place; the best plan is to begin over again and observe care in details. Assiduous stirring or shaking is of no avail in trying to save a "cracked" emulsion, which has a pearly appearance in the mortar, and the further addition of gum, while increasing the density of the mixture, does not always remedy the trouble.

The above methods are equally well adapted for liquid oleoresins, such as copaiba, oleoresin of cubeb, etc. If solid fats, camphor, some oleoresins and resinous extracts, as, for instance, extract of Indian cannabis, are to be administered in aqueous liquids, it will be found advantageous to dissolve them in a small quantity of fixed oil (oil of sweet almond or olive oil), and then to emulsify them in the manner directed for these oils. Salol, menthol, thymol, phosphorus, and other substances, can likewise be conveniently emulsified after solution in some fixed oil. The emulsification of Peru balsam will be materially facilitated by the addition of a little alcohol or oil of sweet almond, about 10 per cent. of the volume of balsam being sufficient. If emulsions of wax or spermaceti are to be made, heat must be employed; the wax or spermaceti is melted in a mortar heated to about 65° C. (149° F.) and mixed with an equal weight of powdered acacia, after which, exactly one and a half times as much water as acacia, heated to near boiling, is added, and the mixture briskly stirred. After the emulsion cools to about 30° C. (86° F.), more water may be added in small quantities, with constant stirring. Whenever double emulsions are ordered, as, for instance, a seed emulsion with that of a fixed oil, better results will be obtained if separate emulsions be made and then mixed; when castor oil is to be mixed with emulsion of almond as a vehicle, the oil should be emulsionized with the requisite quantity of acacia and water, and this primary emulsion then diluted with the almond emulsion, out of which the water necessary for the previous emulsification of the oil has been retained.

Castor

Whenever an oil emulsion is made, the rule should be observed never to measure the water in an oily graduate, as otherwise oil particles might be subsequently carried into the mixture, and, failing to be emulsified, eventually rise to the surface. The view held by some authorities, that a good emulsion is capable of emulsifying additional quantities of oil, requires modification, as already pointed out by Mr. Gerrard, of England; for, although a perfect fixed-oil emulsion admits of the incorporation of more oil, this latter oil will not undergo emulsification, but be simply intimately mixed, as can be proven by the addition of water, when the newly added oil will separate. A perfect artificial emulsion should have a milk-like appearance and consistence, be miscible with water without separation, should flow readily from the mortar without leaving any adhering particles, so that it can be washed with plain water, and, if separation takes place after standing at rest for some time, a cream-like layer should rise to the surface, which can be quickly reincorporated by agitation. Heat is detrimental to the permanence of emulsions and causes separation, so also large quantities of alcohol or saline matter. Substances which have a tendency to absorb water, such as magnesia, must not be mixed with the emulsion, unless previously completely hydrated. All salts should be added in the form of solution, and together with tinctures and other alcoholic liquids, not until the primary emulsion has been properly diluted.

Emulsions of ether, chloroform, oil of turpentine, and other volatile liquids, are best prepared by agitation in a bottle after the manner first suggested by Forbes. The liquid to be emulsionized is poured into a *perfectly dry* bottle and the powdered acacia added, after which the bottle is well shaken so that the acacia may become saturated with the volatile liquid; water is then added and agitation continued until a homogeneous emulsion results, which can be further diluted by the gradual addition of water. Volatile oils and ethereal liquids will never form as perfect an emulsion as fixed oils, and separation of the mixture takes place more speedily; if care has been observed, however, in making the mixture, only a dense creamy layer will rise to the surface, which can be reincorporated by agitation. As a rule, volatile oils and ethers require more gum than fixed oils, and less than 30 grains of powdered acacia should not be used for each fluidrachm; the amount of water first added should always be equal to twice the acacia used. Oil of turpentine unites very readily with water and gum, and it is surprising to see how small a quantity of gum will suffice to form a perfect emulsion from which no oil will separate in an uncombined form, only a dense creamy layer rising, composed of the oil of turpentine, gum, and some water in intimate union; 20 grains of powdered acacia shaken in a bottle with 1 fluidounce of oil of turpentine, and 4 fluidrachms of water then added, will yield a very satisfactory emulsion, which can be kept for days without separating an oily layer. All emulsions of volatile oils are more permanent if made with the aid of some fixed

oil previously added to the volatile oil; such emulsions are preferably made in a mortar.

When powdered tragacanth is preferred as an emulsifying agent, it may be used in the proportion of one-tenth or one-eighth of the necessary weight of acacia, and requires from 10 to 20 times its weight of water; it should be thoroughly mixed with the oil in the mortar or bottle, as the case may be, and after the addition of water the mixture should be rapidly stirred or shaken until the primary emulsion has been formed. The division of oil globules by means of mucilage of tragacanth is much coarser than with acacia, hence tragacanth emulsions are never so white nor seemingly so perfect; but owing to the viscosity and magma-like condition of mucilage of tragacanth, the oil globules, although not finely divided, are kept from re-uniting, and thus separation of an oily layer is prevented. Mixtures of tragacanth and acacia are often employed, particularly in the emulsification of cod-liver oil, to obtain greater protection against separation.

Yelk of egg has long been known as a valuable excipient in emulsions, particularly when acids or large proportions of alcoholic liquids are to be added. One yelk from an egg of average size will suffice for 1 fluidounce of a fixed oil or for ½ fluidounce of a volatile oil; in place of the simple yelk, the official glycerite of yelk of egg, also known as glyconin, of which ½ fluidounce is necessary for an ounce of fixed oil, has been used with decided advantage. In either case the oil should be added in small quantities to the yelk of egg or glyconin, previously rubbed smooth in a mortar, each portion being thoroughly incorparated before another addition is made; if the mixture should become inconveniently thick, a small quantity of water may be introduced, and after all the oil has been emulsified the prescribed amount of water is added, likewise in divided portions, with constant stirring. The readiness with which yelk of egg unites with fixed oils is due to the fact that it is itself a natural emulsion of an oil and albuminous matter. Some little care is necessary in removing the yelk of egg from the shell, to avoid contamination with the white or albumen, which has a tendency to form clots in the emulsions.

Among other emulsifying agents introduced during the last ten years, none has been more extensively used, particularly on a large scale by manufacturers, than mucilage of Irish moss. Toward fixed oils the mucilaginous matter of Irish moss behaves somewhat like tragacanth, particularly if the solution of the former be made somewhat thick. This mucilage is made by washing the drug with cold water to remove saline and other foreign matter, then heating it with the required quantity of water in a dish, for fifteen minutes, on a boiling water bath, and finally straining the mixture; the strength of the mucilage may be from 10–15 grains to the ounce, that of the *National Formulary* being 12 grains. Of the latter mucilage, 1 fluidounce is considered sufficient for 1 fluidounce of oil, the emulsion being made by adding the oil in small portions to the mucilage contained in a bottle and agitating briskly after each addition; after all

the oil has been emulsified, syrup or more water may be added as a diluent. Emulsions made with Irish moss are not so white as those made with acacia and contain the oil in a coarser state of division; some manufacturers add acacia to the Irish moss mucilage, in order to improve the emulsion.

While milk itself is a very poor emulsifier of fats and fixed oils, its albuminoid constituent, casein, is said to be even superior to acacia. According to Leger, a French pharmacist, it is best used in the form of a saccharated powder, prepared as follows: To 4 quarts of milk warmed to 40° C. (104° F.) add 2¼ fluidounces of ammonia water, and after setting aside for twenty-four hours, withdraw the lower milk-serum from the upper fatty layer. Precipitate the casein from the milk-serum by addition of acetic acid, and wash the precipitate by decantation with water warmed to about 40° C. (104° F.); finally collect on a wetted muslin strainer and express the moisture. Determine the amount of dry casein in the residue by heating a weighed portion to complete dryness in an air-bath; add 10 grammes of sodium bicarbonate and sufficient sugar to obtain, when dry, a powder containing 10 per cent. of its weight of casein. The mass must be dried at a gentle heat and powdered; it keeps well for a long time in securely corked bottles. For oil emulsions, Leger recommends the making of a mucilage of 15 parts of saccharated casein with 5 parts of water, and adding to this in small portions 15 parts of oil, stirring well after each addition; finally diluting the emulsion as required.

Condensed milk has also been successfully used as an emulsifying agent for castor oil and cod-liver oil. A fluidounce of the oil is mixed by trituration in a mortar, in small quantities, with one-half fluidounce of condensed milk, and, when emulsified, one-half fluidounce of water is slowly added, with constant stirring. Such emulsions, however, do not bear dilution well.

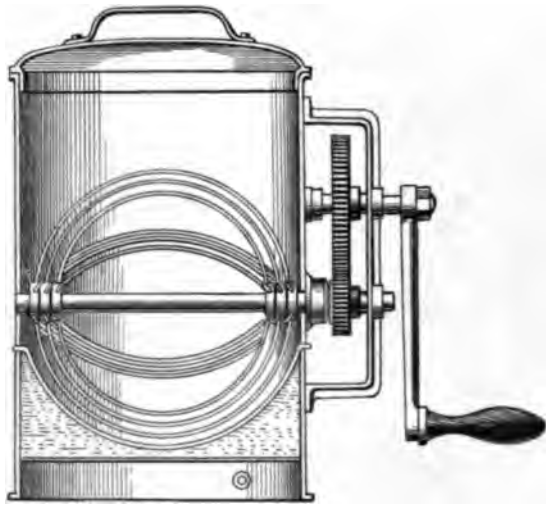
Another emulsifying agent, recommended as a substitute for acacia by some pharmacists, is mucilage of dextrin, to be used in the proportion of 5 or 6 fluidrachms to 1 fluidounce of fixed oil. The mucilage, according to the *National Formulary*, is made by heating 1 ounce of *white* dextrin with 2 ounces of water to near boiling until the dextrin is dissolved; any loss of water by evaporation is made up so that the product weighs 3 ounces; when the mucilage has cooled short of gelatinizing, it is ready for use in the same manner as mucilage of Irish moss.

The saponaceous principle of quillaja possesses the property of dividing and suspending oil globules quite well if used in sufficient quantity. The official tincture of soap-bark may be employed in the proportion of 2 fluidrachms for each fluidounce of fixed oil, or of one-half to one fluidounce for each fluidounce of volatile oil, but owing to the irritant properties of quillaja, it must be used with care, and therefore cannot be recommended for use indiscriminately.

For making from one to five gallons of emulsion, the apparatus

known as the Morton Patent Egg-Beater or Whisking Machine, illustrated in Fig. 205, has been found very serviceable and satisfactory; it is made of heavily-tinned iron, and supplied with a water-chamber underneath, by means of which either hot or cold water may be employed for tempering, whenever desired. The upper tank is provided with a rounded bottom, and the emulsification is effected by means of several heavy wire beaters in circular form revolving rapidly in opposite directions within each other, whereby constant cross-cutting of the mixture and most perfect dashing of the constituents is insured; to prevent dust from entering, the tank is provided with a well-fitting top. The beaters are easily removed by withdrawing the frame, and the apparatus can be quickly and thoroughly cleaned.

FIG 205.



The Morton Patent Egg-Beater.

When emulsions are to be made on a large scale, the usual plan is to add the oil, in a thin continuous stream, to the mucilage contained in a suitable churning apparatus operated by steam power, the mixture being kept in constant agitation by rapidly revolving metallic blades frequently provided with numerous perforations. In this way, 10 or 15 gallons of oil can be completely emulsified in the course of a day.

The Official Emulsions.

The Pharmacopœia recognizes four emulsions: one made from seed, two from gum-resins and one containing chloroform together with a fixed oil. In each case specific directions are given for manipulation, which agree with those explained elsewhere.

ALPHABETICAL LIST OF THE OFFICIAL EMULSIONS.

Official Name.	Composition.	
Emulsum Ammoniaci	Ammoniac	4 Gm.
	Water, sufficient to make	100 Cc.
Emulsum Amygdalæ	Sweet Almond	6 Gm.
	Acacia	1 "
	Sugar	3 "
	Water, sufficient to make	100 Cc.
Emulsum Asafœtidæ	Asafetida	4 Gm.
	Water, sufficient to make	100 Cc
Emulsum Chloroformi	Chloroform	4 "
	Expressed Oil of Almond	6 "
	Tragacanth	1.5 Gm.
	Water, sufficient to make	100 Cc.

Special Remarks.

Emulsion of Almond. The acacia and sugar prescribed in the official formula are by no means essential to the formation of a perfect emulsion, although they add to the stability of the preparation. Emulsion of almond more closely resembles cow's milk in appearance than any other seed or oil emulsion made; the fixed oil present is kept suspended in a very fine state of division, by means of the albuminous matter known as emulsin or synaptase, which constitutes the chief body of the seed. Blanched almonds should always be used, so that a pure white liquid may result. Almonds are best blanched by macerating them in warm water until the skin becomes loose, when it can be quickly removed by simple pressure between the fingers. Emulsion of almond should always be made fresh when wanted.

Emulsion of Chloroform. The official formula yields a stable emulsion, from which neither chloroform nor oil separates even in a week's time, but, since the preparation is never kept in stock, a smaller quantity of tragacanth will prove equally efficacious, and I should prefer to reduce it to two-thirds of the prescribed quantity, which yields a more fluid but very satisfactory emulsion.

CHAPTER XXVII.

MIXTURES.

THE term "mixture" in pharmacy, and more particularly in dispensing operations, is applied to liquid medicines which either contain insoluble substances in suspension or are composed of two or more liquids, with or without the addition of saline or other material in solution; in its more restricted application the term is applied to such medicines as are intended for internal administration. In only a few cases, in which the stability of the preparation for a considerable length of time can be reasonably assured, are mixtures kept in stock; hence the extemporaneous preparation of mixtures is a matter of constant occurrence, as it is a favorite method of administering medicines with physicians, because more extended use can be made of excipients and flavoring agents, with the view of improving the mixture pharmaceutically and therapeutically. Considerable skill and judgment are frequently necessary in the preparation of mixtures, so that the object of the prescriber may be fully attained and each fraction of the mixture contain an aliquot part of all the ingredients. All insoluble or only partly soluble substances, particularly those of a vegetable nature, should be brought to the condition of smooth and uniform suspension, by trituration in the form of very fine powder with the liquid in the mortar; this is best done by first rubbing into a smooth paste with a portion of the liquid and then diluting this with the remainder, constantly stirring. Calcined magnesia or magnesia and charcoal can best be brought into a uniform mixture with water, by stirring at once with sufficient water to overcome the tendency of the magnesia to "set" in a gelatinous mass; a *small* quantity of water added to calcined magnesia also causes it to become gritty and difficult to mix. Some prefer to add the magnesia to the water and diffuse by agitation. In all cases the mixture should be passed through a loosely textured cloth. All powerful remedies, such as mercuric chloride, arsenous acid, the salts of morphine, strychnine, etc., should always be brought to a state of solution before they are added to the other ingredients of a mixture, so as to insure a uniform distribution throughout the liquid. Substances which are readily diffusible in the liquid by agitation of the bottle, do not, as a rule, require the addition of an excipient to insure their uniform suspension, but other insoluble substances which are relatively much heavier than water, or are inclined to float on the surface of the liquid, demand the addition of some mucilaginous or other body to increase the density. Syrup, glycerin, or honey is frequently prefer-

able to acacia or tragacanth, especially in the case of heavy metallic salts, liable to form, with the gum, a compact mass, which cannot be readily suspended by agitation.

Formerly emulsions were recognized among the mixtures, but they are now considered as a distinct class of preparations, the characteristics of which have been described in the preceding chapter.

In connection with the preparation of mixtures, it becomes necessary to consider the subject of incompatibility; this term is applied to the antagonism or disability of harmonious coexistence, which is exhibited by numerous substances when brought into contact with certain other substances. Liquids which are not mutually intersoluble, although they can be brought into homogeneous mixture with the aid of excipients, are often said to be incompatible with each other, as in the case of fixed oils and water, chloroform and glycerin, etc.; but, strictly speaking, the term incompatibility in pharmacy refers to the relation existing between two or more bodies, by reason of which they cannot be mixed without undergoing or producing some change of a physical or chemical nature. Three kinds of incompatibility exist—pharmaceutical, chemical, and therapeutical, of which the pharmacist must take note, and for the proper understanding of which he must rely upon his knowledge of the physical, chemical, and medical properties of drugs.

PHARMACEUTICAL INCOMPATIBILITY is such as effects the physical properties of substances, and is chiefly confined to their solubility; it may result in the partial or total separation of matter held in solution, which may include valuable constituents of the mixture, or it may simply cause a separation of liquids from each other. The changes due to pharmaceutical incompatibility, being entirely of a physical character, can often be avoided or overcome by judicious manipulation or by the addition of some suitable excipient or protective agent. The mixture of strongly alcoholic liquids with solutions of acacia—of acid or neutral aqueous liquids with resinous tinctures—of alcoholic or ethereal solutions of volatile oils and other substances with aqueous liquids—the admixture of solids which undergo liquefaction by reason of intersolubility, as in the case of camphor with solid fats, chloral hydrate, thymol, salol, menthol, etc.—the addition of certain metallic salts to vegetable solutions, causing gelatinization, as in the case of tincture of ferric chloride and mucilage of acacia—are all instances of pharmaceutical incompatibilities. In many cases of physical incompatibility, the trouble may be averted by appropriate dilution before mixing, as for instance, when spirit of nitrous ether or tincture of ferric chloride is to be mixed with a strong mucilage of acacia: a perfectly harmonious mixture, free from precipitate or gelatinization, can be prepared if the mucilage as well as the spirit or tincture be first largely diluted with water, and such should be the invariable rule when these substances are prescribed together. When tinctures of asafetida, guaiac, lupulin, myrrh, and similar substances are ordered in combination with aqueous saline liquids,

separation of the resinous matter will invariably result, unless a protective agent is present, by means of which the finely divided precipitate is kept in perfect suspension. Syrups and glycerin are frequently associated with resinous tinctures by physicians, for the purpose of avoiding the separation of resin, and, if used in sufficient quantity, will answer the purpose; in the absence, however, of such provision, it is the duty of the pharmacist to add some inert substance which will enable him to prepare a mixture of uniform composition. If the following two prescriptions be dispensed exactly as ordered, the resin of the tincture in both cases would be precipitated and gradually deposited on the sides and bottom of the bottle, thus depriving the patient of an important part of the medicine; no amount of shaking will even temporarily suspend the precipitated resin uniformly, but only increase its separation from the liquid.

℞.—Potassii Bromidi . .	℥iv.	℞.—Potassii Chloratis .	℥ij.
Tinct. Lupulini . .	℥j.	Tinct. Guaiaci . .	℥j.
Aquæ Menthæ Vir. .	℥ij.—M.	Aquæ . . q. s. ad	℥iv.—M.

By mixing the resinous tincture or fluid extract with powdered tragacanth in a mortar, and then adding the water or saline solution gradually, with constant stirring, a perfect mixture can be obtained from which the suspended resin separates very slowly in a finely divided form, so as to be readily reincorporated by simple agitation. The proportion of tragacanth to be used will depend, to some extent, upon the volume of dilution; for instance, in the above prescriptions, 10 or 12 grains will be amply sufficient, whilst if a 6 oz mixture were intended 15 or 18 grains would be preferable. As a rule, 10 grains of tragacanth will be required for each fluidounce of a tincture or half fluidounce of a fluid extract.

The turbidity caused by the partial separation of volatile oil or other bodies when an alcoholic solution of the same is added to aqueous fluids, is due to the decreased solubility of the substance in the diluted spirit and cannot be overcome by the ordinary methods; filtration with the aid of such media as purified talcum, calcium phosphate, etc., is not always permissible, and then the application of the general rule—*never to dispense a mixture containing insoluble matter without a "Shake well before using" label*—is all that can be done by the pharmacist.

Chemical Incompatibility, as its name indicates, depends upon the chemical properties of substances, and invariably involves decomposition of one or all of the bodies brought into contact, with the resulting formation of new compounds. The existence of chemical incompatibility has proven most valuable in the study of inorganic and organic matter, and forms the basis upon which rests the very extensive superstructure of analytical chemistry. Chemical decomposition is not always accompanied by the separation of insoluble matter, for, in numerous cases, the newly formed compound is perfectly soluble in the liquid present. Among the most dangerous

incompatibles are mixtures of the chlorates or permanganates with readily oxidizable substances, hence particular care must be exercised in bringing the former into intimate contact with organic matter, so as to avoid possible serious explosions.

There are different conditions under which chemical incompatibility manifests itself, chief among which are the following:

1. Two salts composed of different acid and basic radicals, when brought together in a state of solution, mutually decompose each other; the resulting new compounds may both remain in solution, in which case no evidence of decomposition is apparent and it scarcely seems proper to consider the two salts used as incompatible with each other, as when solutions of ammonium chloride and potassium iodide are mixed, or those of cupric sulphate and zinc acetate. When, however, one of the new compounds is insoluble in the liquid and is deposited as a precipitate, true incompatibility has been established; as in the case of a mixture of solutions of lead nitrate and potassium iodide, lead iodide being precipitated. Sometimes the new insoluble compound enters into union and solution with one of the original substances, if the latter is present in excess, in which case the chemical incompatibility of the original two substances remains, and the resolution of the insoluble compound must be looked upon as a new operation. Such examples are presented by mercuric chloride and potassium iodide, if either salt is in excess, or by potassium cyanide and silver nitrate, the former salt being in excess.

2. Salts of the heavy metals, and, in many instances, also those of the alkaline earths and earths, are decomposed by the alkalies or their carbonates, forming insoluble compounds, hence incompatibility exists between such salts. As examples may be mentioned mercuric chloride with potassium hydroxide, lime-water with sodium bicarbonate, calcium chloride with potassium carbonate and alum with sodium carbonate.

Bismuth subnitrate is frequently prescribed in a mixture with sodium bicarbonate, and almost invariably decomposition takes place, resulting in a more or less violent disengagement of carbon dioxide; as the reaction takes place slowly, at times it may not occur until the mixture has been transferred to a bottle and corked. The remedy lies either in using the bismuth subcarbonate in place of the subnitrate, or in mixing the subnitrate and bicarbonate in a mortar and adding a little boiling water, so as to hasten and complete the reaction.

3. When oxidizing agents are brought into direct contact with organic matter, chemical reaction at once ensues, which is often of a violent nature, and is among the most important incompatibilities met with. To this class belongs the trituration of potassium chlorate with sulphur, sugar, tannin, or acacia; the solution of chromic acid or potassium permanganate with glycerin, etc.

4. The association of the salts of gold and silver with reducing agents gives rise to an exhibition of incompatibility, by converting

the gold and silver to the metallic state, thereby rendering them less soluble. All organic matter has a decomposing effect upon the compounds of gold and silver, but more particularly glucose, honey, syrup, and glycerin; hence these should be avoided in prescriptions.

5. Salts when brought in contact, either in the dry state or in solution, with acids or bases stronger than their own acid or basic radicals, will suffer decomposition, the result being new compounds with the evolution of the old acid or base. If the liberated acid or base be volatile, it will be given off in gaseous form, and may cause serious annoyance to the dispenser unless proper precautions be observed. The preparation of the official solution of ammonium acetate proves the incompatibility of all carbonates with acids, and the development of ammoniacal vapors when ammonium salts are triturated with potassa proves the incompatibility of salts with stronger bases.

Whenever carbonates are prescribed with an acid liquid, the dispenser should allow the reaction to be completed before corking the vial, so that the greater portion of the gas may escape, and caution the patient to keep the vial in a cool place and not violently agitate it. If a viscid or saponaceous liquid is also to be added, as mucilage or syrup of senega, it is all the more important that chemical reaction be allowed to subside before the addition is made, and that as little carbon dioxide as possible be kept in the solution.

With some physicians, the following is a favorite prescription:

℞.—Ammonii Carbonatis	āā	℥j.
Ammonii Chloridi		
Syrupi Scillæ	āā	℥j.
Syrupi Senegæ		
Syrupi Tolutani		℥ij.

Ft. sol.

The proper way of mixing these ingredients is to rub the salts to a fine powder, and add to them, *while in the mortar*, the syrups of squill and tolu previously mixed, stirring the mixture with the pestle *until effervescence ceases;* finally add the syrup of senega. If a persistent froth forms on the surface of the liquid, this may be quickly dispelled by carefully sprinkling a few drops of alcohol over it, before the mixture is transferred to a bottle.

To this class of incompatibilities belongs also the decomposition and precipitation caused in fluid extract of liquorice by acids; the sweet principle in liquorice is ammonium glycyrrhizate, which, upon addition of dilute sulphuric or other acid, is decomposed, the glycyrrhizin being deposited on the sides and bottom of the vessel. Physicians sometimes prescribe an acid solution of quinine, together with fluid extract of liquorice, in the hope of disguising the bitter taste, overlooking the fact that the bitter taste of quinine is always intensified by bringing the latter into solution. As the intended effect of the liquorice is defeated by the presence of an acid, there is but one course open to the pharmacist with prescriptions of this kind, namely, to omit the acid, triturate the quinine with the fluid extract or syrup

of liquorice, and dispense the mixture with a "Shake well before using" label. It is advisable, at the same time, to explain to the physician what has been done, giving the reason therefor, so as to avoid, if possible, a repetition of the blunder.

The decomposition of salts by stronger acids or bases is frequently resorted to intentionally, as in the well-known "Neutral Mixture," made from lemon juice and potassium bicarbonate, and in "Preston or Smelling Salts," composed of ammonium chloride and lime, usually flavored with oil of lemon and oil of lavender.

6. The salts of the alkaloids are decomposed by certain salts of the alkalies, with the production of insoluble or sparingly soluble compounds, therefore such combinations require the special attention of pharmacists in order to guard against accidents. As a rule, the alkali carbonates, iodides, and bromides are incompatible with alkaloidal salts, while the sulphates, nitrates and chlorides appear to cause no trouble; hence in the case of the first-named salts the directions to shake the mixture should always be put on the bottle. In a few rare cases, when a sufficient quantity of solvent is present to take up the alkaloid in its pure state, it may be preferable to use the latter in place of its salt, as, for instance, in the following prescription:

℞.—Codeinæ Sulphatis	. . . . .	gr. viij.
Potassii Bromidi	. . . . .	℥j.
Aquæ destillatæ	. . . . . q. s. ut ft.	℥iv.

Ft. sol.

It was found that if the codeine sulphate was used, as prescribed, a precipitate invariably formed, which was with difficulty uniformly suspended by agitation, but by using the pure alkaloid codeine in place of the salt, a permanently clear solution was obtained. Morphine sulphate is sometimes prescribed in conjunction with sodium bicarbonate, the result being a minutely crystalline precipitate. Quinine sulphate and potassium acetate should not be associated in solution, on account of the slight solubility of the quinine acetate, which is formed as a very bulky precipitate and may cause solidification of the mixture.

7. Vegetable astringents are incompatible with alkaloids, glucosides, albumen, gelatin, and many metallic salts; in some cases, curdy precipitates are formed, which afterward adhere to the sides of the vessels, while in other cases light, readily diffusible precipitates are obtained, or possibly only turbidity or discoloration ensues. The character of such a mixture depends, to some extent, upon the degree of dilution and the presence of other bodies. Quinine and tannin are sometimes prescribed together, but should never be triturated with water, as a tough insoluble mass would at once be formed; the two substances are best mixed with syrup and afterward diluted with water, if desired, when the insoluble quinine tannate can be readily suspended by simple agitation. The formation of ink depends upon the incompatibility of tannin with iron salts, and is a fruitful source

of annoyance to the pharmacist. The value of strong coffee and tea or similar astringent infusions as antidotes for metallic poisoning, is due to the formation of sparingly soluble compounds. Vegetable astringents have been found incompatible also with spirit of nitrous ether, several explosions having occurred from mixing the latter with the fluid extracts of uva ursi, matico, geranium, and even gentian; the gas liberated by these reactions appeared heavily charged with some nitrous compound.

The presence of certain protective agents has been known to avert, or at least to modify, the chemical decomposition between some substances; in such cases it is, of course, essential that the protective agent be mixed with one of the substances before the other is added. The following examples will show the action of glycerin, acacia, and syrup, in this respect. Physicians frequently prescribe cocaine hydrochloride or morphine salts in solution, together with borax, which causes precipitation and thus unfits the solution for use; the addition of a little glycerin prevents the decomposition. Zinc chloride and borax, prescribed together in solution, will cause the formation of insoluble zinc borate, which is prevented, however, by the presence of glycerin; strange to say, such a clear solution containing glycerin will bear further dilution with water only up to a certain point, beyond which precipitation ensues. The exact action of the glycerin in the foregoing cases is not clearly understood, but, reasoning from the effect of glycerin on borax alone, it may be assumed that a similar action obtains in the mixture with alkaloidal and other salts, the glycerin decomposing the borax, by liberating a part of the boric acid, which itself is perfectly compatible with the salts above mentioned, as has been shown by making the solutions with boric acid instead of borax or borax and glycerin. On the other hand, glycerin may sometimes act as a disturbing agent and cause decomposition which otherwise would not occur. Borax and sodium bicarbonate are perfectly compatible in aqueous solution, and are frequently prescribed together; if glycerin be present, reaction is set up by the boric acid liberated from the borax, and the sodium bicarbonate is decomposed with copious evolution of carbon dioxide. Such a mixture must be made in a mortar and the reaction allowed to subside before bottling it.

Corrosive mercuric chloride and lime-water are known to be incompatible, but are often ordered together with the view of utilizing the freshly-formed yellow mercuric oxide in moist condition; mercuric chloride will also precipitate acacia from a strong solution, but, if a dilute solution of mercuric chloride be added to mucilage of acacia and subsequently mixed with lime-water, no precipitate whatever will occur for several days, when finally a grayish deposit of finely divided metallic mercury or mercurous oxide is formed. When a physician orders such a combination as mercuric chloride, water, mucilage of acacia, and lime-water, the object is plainly to keep the mercuric oxide better suspended, and the mixture should be made by

adding the mucilage last of all, after decomposition of the mercuric chloride has been completed.

Chemical incompatibility may result in rendering a mixture less active or even inert from the formation of insoluble compounds, as when tartar emetic is ordered in combination with syrup of wild cherry or tincture of digitalis with tincture of cinnamon, etc.; on the other hand, the medicinal activity of the mixture may be intensified by the formation of poisonous compounds, as in the case of mercurous iodide with soluble iodides, producing mercuric iodide and metallic mercury, or the association of calomel with soluble chlorides or iodides, etc. In all such cases the pharmacist should consult the prescriber and acquaint him with the prospective results.

It must not be supposed, however, that because precipitation occurs as a result of chemical incompatibility, the mixture is always rendered inert thereby; the decomposition is often intentional with a view to obtaining the insoluble compound in a freshly formed and more active condition. Such instances are found in the well-known "black wash" and "yellow wash" (prepared from lime-water with calomel and corrosive sublimate respectively), in the mixture of solutions of tannin and of lead subacetate, which produce a magma-like precipitate of lead tannate, and in the frequently prescribed mixture of zinc sulphate with a solution of lead acetate, giving the freshly precipitated lead sulphate, which is much preferred. The official compound iron mixture is another instance of intentional decomposition, the newly formed ferrous carbonate being the object sought. It requires no little judgment on the part of the pharmacist to discern when the prescriber intentionally orders chemically incompatible substances together, or when this happens from a want of familiarity with chemical reactions.

THERAPEUTICAL INCOMPATIBILITY depends entirely upon the antagonism existing between drugs in regard to their physiological effect or medical action, and does not properly belong to the domain of pharmacy; the remedy for such a condition lies solely in the hands of the physician, who is supposed to be familiar with the requirements of his patients and the therapeutical action of drugs. Sometimes the intended medicinal effect of a substance is destroyed by chemical action, as when ammonium carbonate is associated with syrup of squill; this, however, cannot be considered as a therapeutical incompatibility.

FIG. 206.

While it is well understood in prescription practice that solutions should always be filtered through a pledget of cotton placed in the throat of a funnel to remove motes and specks, the rule should also prevail, in dispensing mixtures, that the mixture be strained through bolting-cloth, in order that the insoluble matter be

free from lumps and in a uniformly divided state; the straining is best accomplished by placing the bolting-cloth between the upper and lower part of a rubber or tin funnel, as shown in Fig. 206, which can be inserted directly into the prescription vial.

The subject of incompatibility is practically an endless one, but the following summary will, to some extent, aid the dispenser in determining the character of numerous mixtures; it must be borne in mind, however, as stated before, that not all incompatibles produce inert or poisonous compounds, and that while in many cases the incompatibility can be overcome by appropriate means, physicians frequently associate incompatible substances for a specific purpose.

SUMMARY OF INCOMPATIBILITIES. (After HAGER.)

Acacia	with ferric chloride, alcohol, borax, lead salts, and ethereal tinctures.
Acids in general	" alkalies, alkaline fluids, acetates, and metallic oxides.
Acid, Arsenous	" lime-water, magnesia, and oxides of iron.
Acid, Carbolic	" potassium permanganate, iodine, bromine, caustic alkalies, and iron salts.
Acid, Chromic	" glycerin, alcohol, ether, essential oils, and organic matter in general.
Acid, Picric	" alkaloidal salts, dry acids, iodine, sulphur, and organic salts. (These incompatibilities extend also to the salts of picric acid.)
Acid, Salicylic	" potassium permanganate, iron salts, lime-water, potassium iodide, and soap. (These incompatibilities extend also to the salts of salicylic acid.) Alkali salicylates will darken unless an excess of acid be present.
Acid, Tannic	" mucilages, tartar emetic, silver nitrate, metallic salts in general, alkaloids and their salts, lime water, potassium chlorate, alkali carbonates and bicarbonates, albumen, gelatin, and chlorine water.
Albumen	" mineral acids, alcohol, mercuric chloride, and vegetable astringents.
Alkaloidal Salts	" borax, tannin, and all vegetable astringents, alkali carbonates, the permanganates, iodides, liquorice, strong mucilages, magnesium carbonate, and alkaline tinctures.
Alum	" alkalies and alkali carbonates.
Ammonium Acetate, Ammonium Bromide	" mineral acids, alkali carbonates, chlorine, potassium chlorate and dichromate, silver nitrate, mercurous chloride and nitrate.
Ammonium Chloride, Ammonium Phosphate	" carbonates of the alkalies and earths.
Amyl Nitrite	" alcohol, tinctures in general, alkali carbonates, calomel, lead salts, potassium iodide, the bromides and ferrous salts.
Antimony, Sulphurated	" sodium bicarbonate, potassium bitartrate, bismuth subnitrate, and calomel.
Antipyrine	" sodium salicylate (dry), calomel, chloral hydrate, spirit of nitrous ether, and nitrites in general.
Apomorphine Hydrochloride	" sodium carbonate and bicarbonate, iodine, tannin, and iron salts.

Barium Chloride	with	sulphuric and phosphoric acids and their salts, carbonates, tartrates, vegetable infusions, and medicinal wines.
Bismuth Subnitrate	"	calomel, tannin, sulphur, and antimony sulphide.
Calcium Chloride	"	calomel, sulphates, phosphates, tartrates, and carbonates.
Calcium Hypophosphite	"	potassium chlorate, iodide, and permanganate; also chlorinated lime. (These incompatibilities extend to all hypophosphites.)
Calomel (Mercurous Chloride)	"	acids, acid salts, alkali carbonates, lime water, ammonium chloride, iodine, potassium iodide, ferrous chloride and iodide, sulphur, bitter-almond water, cherry-laurel water, antimony sulphide, and antipyrine.
Chloral Hydrate	"	water (slow decomposition), warm water, alkali carbonates and organic salts, calomel, potassium cyanide, antipyrine, salts of ammonium, mercurous nitrate, permanganates, alcohol, tinctures in general, bromides, and iodides.
Chlorine Water	"	alkalies and their carbonates, ammonium salts, salts of the organic acids, lead salts, silver nitrate, mucilages, tannin, extracts, tinctures, infusions, emulsions, and milk.
Corrosive Sublimate (Mercuric Chloride)	"	lime-water, soap, iodine, opium, potassium iodide, organic acids, tannin, and alkali carbonates.
Digitalis	"	tannin, lead acetate, iodine, potassium iodide, iron salts, and alkali carbonates.
Iodine	"	ammonia, starch, metallic salts, fatty and volatile oils, emulsions, carbolic acid, chloral hydrate, acacia, tragacanth, magnesium, carbonates, and sodium thiosulphate (hyposulphites.)
Iodoform	"	silver and other nitrates, potassium chlorate, nitrites, and mineral acids. The modification or destruction of the odor of iodoform by the following substances points to incompatibility: tannin, Peru balsam, tincture of myrrh, naphtalene, cumarin, and the volatile oils of anise, bergamot, fennel, peppermint, and turpentine.)
Iron, Reduced	"	aloes, tannin, infusions, extracts, metallic and alkaloidal salts
Iron Salts	"	alkali carbonates and bicarbonates, mucilages tannin, infusions, extracts, and astringent tinctures
Lead Acetate (also Lead Subacetate	"	opium, lime-water, ammonium chloride, alum, potassium iodide, iodine, acacia, tragacanth, tannin, carbonates and sulphates, and sulphuric and hydrochloric acids. Normal lead acetate is compatible with mucilage of acacia, but the basic or subacetate causes precipitates, even in minute quantities
Lime, Chlorinated	"	ammonium chloride, sulphur, tannin, metallic sulphides, glycerin, volatile oils, and fatty substances.
Lime-water	"	acids, ammonium salts, carbonates, tartrates, metallic salts, tannin, infusions, and many tinctures.
Morphine Salts	"	the salts of iron, manganese, and silver, potassium chlorate and permanganate, nitrites and nitrates, carbonates of the alkalies and the earths, amyl nitrite and bitter-almond water

Musk	with	acids, acetates, tannin, ergot, and metallic salts.
Opium, including the Tincture and Extract of Opium	"	alkali carbonates, tannin, metallic salts, iodine, chlorine water, and the preparations of nux vomica and belladonna
Pepsin	"	alkaline substances, alcohol, and tinctures in general.
Potassium Bromide	"	mineral acids, chlorine water, and the salts of mercury and silver.
Potassium Chlorate	"	mineral acids, tannin, catechu, sulphur, charcoal, calomel, sulphites, ferrous salts, nitrites, hypophosphites, sugar, honey, and vegetable powders.
Potassium Iodide	"	acids and acid salts, alkaloidal salts, silver nitrate, ferric salts, potassium chlorate, spirit of nitrous ether, and salts of lead and mercury.
Potassium Permanganate	"	fatty and volatile oils, alcohol, glycerin, ammonia and ammonium salts, alkaloids, sulphur, charcoal, and organic substances in general.
Silver Nitrate	"	hydrochloric, sulphuric, acetic, and tartaric acids and their salts, hydrocyanic acid, iodine, potassium iodide and bromide, antimony, sulphide, sulphur, tannin, alkali carbonates, carbonates of the earths, and astringent tinctures.
Sodium Bicarbonate	"	acids and acid salts, tannin, metallic and alkaloidal salts.
Tartar Emetic	"	acids and alkalies, calomel, tannin, soap, acacia, opium, and vegetable astringents.

In Europe, effervescing mixtures are often prescribed under the name "Saturations," which are made by adding to lemon-juice, vinegar, tartaric or citric acid solution, sufficient of an alkali carbonate to produce a neutral or nearly neutral salt, the liquid retaining in solution a large portion of the carbon dioxide evolved, which adds materially to the refreshing taste of the mixture. In the Pharmacopœia will be found a complete table of the quantity of different alkalies and alkali carbonates necessary to neutralize 100 parts of the various official acids.

The Official Mixtures.

Of the four preparations recognized as mixtures in the present Pharmacopœia, only two are fit to be kept on hand for several days or longer, in warm weather; the other two should be freshly made when needed, owing to their rapid deterioration.

TABLE OF THE OFFICIAL MIXTURES.

Name.	Composition.	
Mistura Cretæ	Compound Chalk Powder	200 Gm.
	Cinnamon Water	400 Cc.
	Water, sufficient to make	1000 "
Mistura Ferri Composita	Ferrous Sulphate, cryst.	6 Gm.
	Myrrh	18 "
	Sugar	18 "
	Potassium Carbonate	8 "
	Spirit of Lavender	60 Cc.
	Rose Water, sufficient to make	1000 "

Name.	Composition.	
Mistura Glycyrrhizæ Composita	Pure Extract of Glycyrrhiza	30 Gm.
	Syrup	50 Cc.
	Mucilage of Acacia	100 "
	Camphorated Tincture of Opium	120 "
	Wine of Antimony	60 "
	Spirit of Nitrous Ether	30 "
	Water, sufficient to make	1000 "
Mistura Rhei et Sodæ	Sodium Bicarbonate	35 Gm.
	Fluid Extract of Rhubarb	15 Cc.
	Fluid Extract of Ipecac	3 "
	Glycerin	350 "
	Spirit of Peppermint	35 "
	Water, sufficient to make	1000 "

Special Remarks.

Mistura Cretæ. The compound chalk powder directed for this preparation is the official powder composed of 3 parts of prepared chalk, 2 parts of acacia, and 5 parts of sugar, the insoluble chalk being kept in suspension by the gum and sugar in solution. Precipitated calcium carbonate must not be used in making this mixture, as it is crystalline and does not make so smooth a preparation, nor remain so perfectly in suspension as the prepared chalk. Chalk mixture should be made in small quantities and kept in a cold place.

Mistura Ferri Composita. The preparation of this mixture presents no difficulty if good tears of myrrh be selected and the directions strictly followed. The reaction between the iron and potassium salts, resulting in the formation of ferrous carbonate and potassium sulphate, takes place in the myrrh emulsion, by which the insoluble ferrous carbonate is kept in suspension fairly well. Unless in full and well-corked bottles, the mixture, at first of a dirty-greenish color, is hardly protected against oxidation by the small quantity of sugar present, therefore should be freshly made when needed. Compound iron mixture is also known as Griffith's mixture, and is sometimes prescribed under that name.

Mistura Glycyrrhizæ Composita. The present official formula differs from that of 1880, in ordering syrup and mucilage in place of sugar and powdered acacia, whereby the preparation of the mixture is expedited. The finished product is rather unsightly and by no means in keeping with modern elegant pharmacy. The formula suggested by Charles Tilyard, in 1860, yields an equally efficient and far handsomer preparation; it prescribes a larger proportion of sugar (by no means a disadvantage), and can be still further improved by the use of purified extract of liquorice, as now ordered by the Pharmacopœia. The formula, as modified and adapted to the proportions of the Pharmacopœia, is as follows: Dissolve 30 Gm. of purified extract of glycyrrhiza in 300 Cc. of water; add 120 Cc. of camphorated tincture of opium, 60 Cc. of antimonial wine, and 30 Cc. of spirit of nitrous ether, and set the mixture aside for twelve or twenty-four hours, with occasional agitation; filter the liquid into

a bottle containing 100 Cc. of mucilage of acacia and 600 Gm. of granulated sugar, and wash the filter with sufficient water to bring the volume of the finished product up to 1000 Cc. The sugar is readily dissolved by agitation, the result being a thin, rich-looking clear syrup which keeps admirably. This preparation is popularly known as "Brown Mixture."

Mistura Rhei et Sodæ. Ordinarily, when fluid extract of rhubarb is mixed with water, copious precipitation of resinous and extractive matter at once ensues, but this is prevented, in the official mixture, by the alkali bicarbonate, and the solution is preserved by the glycerin subsequently added. It keeps quite well, but is not often prescribed.

CHAPTER XXVIII.

PILLS.

PILLS are a very convenient mode of administering medicines, the chief advantage lying in the small bulk to which the medicine is reduced and the almost complete disguise of bitter and nauseous remedies, by reason of their being swallowed without previous mastication. Pills are admirably adapted for the administration of heavy metallic substances not readily suspended in liquids, and also in cases in which the action of the medicine is to be slow, or even retarded until it reaches the lower bowels. The usual shape given to pills is that of a sphere or globe, although an ovoid shape is also sometimes used, and, in a few cases, even the lenticular shape is preferred. Their weight ranges from less than 0.06 Gm. to 0.3 Gm. (1 gr. to 5 gr.) for vegetable substances, or about 0.5 or 0.6 Gm. (8 to 10 grains) for heavy mineral compounds; if a pill exceeds this weight it is called a *bolus*. Boluses are occasionally made weighing 1.3 or 2.0 Gm. (20 or 30 grains) each and are often of a softer consistence than pills. Very small pills coated with sugar, are called *granules*.

Although of late years the extemporaneous preparation of pills has materially decreased, and in some localities has almost entirely disappeared, the operation must yet be considered one of the most important pharmaceutical manipulations, and is deserving of a lengthy discussion, because the opportunities for a practical acquaintance with the details of the work are growing less day by day, owing to the untiring efforts of manufacturers to induce physicians to specify factory-made pills on their prescriptions.

The most important step in the preparation of pills is the formation of a proper mass, which should consist of a paste, sufficiently plastic to admit of being moulded without adhering to the moulds, yet firm enough to prevent the pills from losing their original shape. Although a firm consistence should characterize every well-made pill mass, its ready disintegration and solution in the fluids of the stomach and bowels, are of paramount importance, and it is essential to so unite the ingredients of a pill-mass that ready separation in the stomach may be assured. Plasticity is that peculiar condition in which adhesiveness and firmness are properly balanced; the former of these properties is due to a partial softness, which enables the particles of the mass to adhere to each other, thus imparting tenacity to the whole. Some substances possess this adhesiveness in themselves, but require the addition of a liquid—water or alcohol—in order to develop it; as, for instance, gums and resinous drugs. Other

substances possess no inherent adhesive properties, and, in such cases, it becomes necessary to impart tenacity to them, by the addition of some adhesive liquid or solid material; such substances are camphor, calomel, bismuth salts, some saline or vegetable powders, reduced iron and the like. Firmness in a pill-mass is as essential as adhesiveness, and, while the latter is brought about by a state of partial solution or fluidity, so, inversely, the insolubility of some particles is necessary for the required firmness. The substances added to pill-masses as adhesive or absorbent agents are known as excipients, and must be employed judiciously, so that the constituents of the mass be not modified in their action nor the bulk unnecessarily increased. After each addition, the mass should be well kneaded, which, itself having a softening influence, by reason of the heat generated, enables the operator to judge of the true condition of the mixture. Whenever possible, all constituents of a pill-mass should be reduced to very fine powder, before the addition of any excipient, as only in this condition can the homogeneity of the mass as well as the subsequent accurate division of doses be assured. Small quantities of potent remedies, such as alkaloids, narcotic extracts, toxic chemicals, etc., are preferably triturated with a little sugar of milk, before mixing them with the other ingredients, to facilitate uniform distribution.

FIG. 207. FIG. 208.

Sectional view of properly-shaped pill mortars.

Whenever substances are ordered in a pill-mass, in quantities which it is impossible or inconvenient to weigh accurately, as for instance, aconitine 0.001 Gm., digitalin 0.003 Gm., veratrine $\frac{1}{32}$ grain, strychnine $\frac{1}{10}$ grain, etc., a dilution of the substance should be made with sugar of milk, in such proportions that a conveniently weighable quantity shall contain the desired amount of the active ingredient. Thus, if 0.001 Gm. of any substance is wanted, carefully triturate 0.010 Gm. of the substance with 0.090 Gm. of sugar of milk (or 0.050 with 0.450 Gm. if more convenient); each 0.010 Gm. of the mixture will then contain $\frac{1}{10}$ of 0.010, or 0.001 Gm. of the medicinal

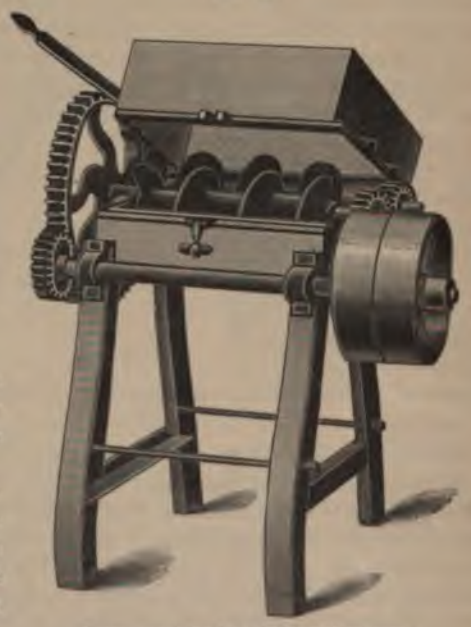
agent. If $\frac{1}{12}$ of a grain of any substance is needed, triturate $\frac{1}{2}$ grain of it with $5\frac{1}{2}$ grains of sugar of milk (or 1 grain with 11 grains), and each grain of the mixture will contain $\frac{1}{12}$ grain, 2 grains will contain $\frac{1}{6}$ grain, or $1\frac{1}{2}$ grains will contain $\frac{1}{8}$ grain of the active ingredient. In like manner any other fractional part of a centigramme or a grain may be readily obtained.

Pill-masses should always be made, according to the nature of the mass, either in iron or Wedgewood mortars, of the shape shown in Figs. 207 and 208, and the mixture should be frequently scraped down with a stiff spatula so as to bring all particles repeatedly together under the pestle. Trituration by means of a pestle is essential to produce a uniform mixture of the ingredients, and moreover it will be found that a mass can be formed in less time, with less excipient and less labor, in a mortar than on a pill-tile; very simple combinations, such as blue mass and extract of colocynth, etc., may be effected on the pill-tile, but, for all substances requiring uniform blending of fine powders, and similar cases, the use of the tile is to be condemned. Unfortunately the misuse of the pill-tile is a characteristic of many American pharmacists. One rule should be strictly observed in making every pill-mass, namely: *Never use the spatula with which the mass is scraped down for taking excipient from its container.*

FIG. 209.

Hand machine for mixing pill-masses.

FIG. 210.



Power machine for mixing pill-masses.

Large quantities of pill-masses which cannot be conveniently handled in the mortar are best made in a special apparatus known as a pill-mixer, operated either by hand or steam-power. As a rule, these kneading machines consist of smooth iron rollers (for white pill-masses hard-wood rollers are generally

used), which revolve in opposite directions, some being so constructed that they can be heated, if necessary, by passing steam through them. The ingredients for the mass are first roughly mixed in a basin or tank and then repeatedly passed between the rollers until a uniform mixture been been produced. In Figs. 209 and 210 are shown two sizes of iron mixers for pill-masses, made by J. H. Day & Co., of Cincinnati, the smaller one having a capacity of three pounds and the larger of thirty pounds. The tanks are porcelain lined, and the corrugated rollers or mixers are galvanized. As shown in the illustrations, the machines are easily opened and taken apart for cleaning purposes. While mixing a mass the rollers turn toward each other, and while emptying, from each other. The finished mass can be easily removed by tilting the machine and at the same time causing the rollers to revolve slowly in a reverse direction.

EXCIPIENTS. It being impossible to select one single substance as an excipient suitable for all pill-masses, owing to the variable properties of drugs and the many different combinations ordered by physicians, it is essential that the pharmacist be familiar with the peculiarities of each excipient, in order to use the same intelligently and advantageously. Excipients for pill-masses may be divided into three distinct classes, as follows:

1. Those which are intended to develop adhesiveness, and hence act as solvents. To this class belong water, alcohol, diluted alcohol, glycerin, and a mixture of glycerin and water.

2. Those which are intended to impart adhesiveness; these may be fluid, semi-fluid, or solid. To this class belong syrup, glucose, honey, mucilage and syrup of acacia, mucilage of tragacanth, glycerite of starch, acacia with glucose or honey, tragacanth with glycerin, soap with water or diluted alcohol, extract of malt, confection of rose, manna and powdered elm bark mixed with tragacanth; the last named requires the addition of syrup or glycerin and water.

3. Those which are intended to act simply as absorbents of excessive moisture and, in a few cases, impart adhesiveness to the mass at the same time. To this class belong powdered liquorice root, soap and liquorice root, calcium phosphate, powdered orris root, powdered tragacanth, powdered elm bark, starch and powdered marshmallow.

The first class, solvents, are employed in many cases in which physicians have ordered vegetable powders in connection with soap or solid extracts, the latter in insufficient quantity to form a good mass. Solvents must be added to pill-masses with great care, especially when water or glycerin is used with soap or extracts; by adding the fluid in drops and working the mass well after each addition, the required consistence will soon be developed, and a firm, yet plastic mass, be obtained, while an excess of moisture causes a softening of the mass, which frequently increases, and prevents the formation of perfect pills, besides requiring the addition of absorbent powders, which add to the bulk of the mass.

The second class, adhesive excipients, are more extensively used than any other, because the majority of substances prescribed in pill form do not possess inherent adhesive properties, or at least insufficiently, for properly massing the ingredients. Mucilage and syrup of acacia are the least desirable of the class, unless the pills are for immediate use, as pills made with acacia are apt in time to become very hard; the addition of glycerin, however, obviates the difficulty. Syrup or glucose is usually preferred to water for massing vegetable powders, in the absence of soap or solid extracts. Tragacanth with glycerin can be most conveniently used in the form of a jelly, made by triturating 85 grains of powdered tragacanth with 6 fluidrachms of glycerin and 1 fluidrachm of water; it is an excellent excipient for the salts of quinine, salol, acetanilid, sodium salicylate, iodoform, calcium sulphide and also gallic and tannic acids, but for cinchonidine sulphate, or salicylate, acacia with glucose or honey is preferable. Soap with water or diluted alcohol, is the best excipient for aloes, rhubarb and the various gum-resins; it cannot, however, be used with soluble metallic salts as those of iron, lead, copper, etc., owing to the formation, by mutual decomposition, of metallic oleates, which cause the mass to crumble.

The necessary precaution regarding the use of water in conjunction with soap has already been mentioned in the preceding paragraph. Manna is very desirable for massing reduced iron or manganese dioxide, when these are prescribed alone. Extract of malt is very similar to glucose in its applicability, but can only be used for dark-colored masses. Confection of rose, at one time much esteemed as an excipient for mixtures of vegetable powder and metallic salts, has now almost gone out of use. For the valerianates of iron, quinine, or zinc, no better excipient can be used than acacia and alcohol in the following proportions: Iron, quinine, or zinc valerianate, 30 grs.; powdered acacia, 10 grs.; alcohol, 5 minims. Camphor and monobromated camphor can be made into very satisfactory pill-masses, by the addition of soap and oil of sweet almond or castor oil; about 1 grain of soap and 2 drops of oil will be sufficient for 12 grains of camphor.

As an excellent adhesive agent for heavy metallic salts, such as bismuth subnitrate or calomel, as well as for the scale salts of iron and troublesome combinations like capsicum, camphor and lead acetate, Mattison's excipient powder will be found very serviceable; it consists of 1 part of powdered tragacanth and 7 parts of finely powdered (No. 80) elm bark. Only a very small proportion of the powder is required, thus: 3 grains for 60 grains of bismuth subnitrate, calomel, cerium oxalate, iron by hydrogen, or equal parts of camphor and lead acetate; 6 grains of the powder for 60 grains of dried ferrous sulphate, the scale salts of iron, or equal parts of camphor and capsicum, etc. In all cases in which this excipient powder is employed, the mass should be made up rather soft with syrup, otherwise it is apt to crack or crumble while the pills are being formed;

pills thus made become sufficiently firm and retain their original shape, on account of the fibrous and adhesive character of the excipient. Hager has recommended a similar powder, composed of 1 part of powdered marshmallow root, 1½ parts of powdered tragacanth, and 6 parts of powdered orris root; this powder can be used like the preceding, and is better adapted to white pill-masses. In place of syrup, a mixture of two volumes of glycerin and one of distilled water may be used for pills which it is desired to keep soft.

At one time, crumb of bread was ordered quite frequently as an excipient for pill-masses, particularly in cases in which it was intended at the same time to serve as a vehicle for the administration of potent remedies, as in the case of mercuric chloride, strychnine, etc. In place of bread-crumb, which is not always available, either of the excipient powders mentioned above may be used, or a mixture of 1 part of tragacanth and 3 parts of starch, the mass to be made with glycerin and water, as before stated. The salts of quinine and cinchonidine are frequently prescribed in pill form, in combination with aromatic or diluted sulphuric acid, the quantity of acid being often left to the judgment of the dispenser. As a rule, from one-third to one-half as much acid as alkaloidal salt, is sufficient to make a satisfactory mass, depending somewhat upon the condition of the atmosphere. The mass must be rolled out as soon as it becomes plastic, while still a little soft, otherwise it becomes dry and crumbly; in the latter case, the addition of a drop or two of syrup, or a very small quantity of glycerite of starch, restores the proper condition. Quinine sulphate triturated with one-sixteenth of its weight of tartaric acid, becomes damp and adhesive, and, upon the further addition of a small quantity of glycerin (about 15 or 16 drops to 100 grains of quinine sulphate), yields an excellent mass, the pills being small and firm. If kept in a cool, dry place, such pills retain their original condition for a long time. Although strong mineral acids are very rarely prescribed in pills, they are occasionally used, in combination with pepsin and vegetable powders, in prescriptions coming from Germany; the excipient powder mentioned in the preceding paragraph, together with glycerin and water, will yield a good mass.

Easily reducible substances, like silver nitrate, potassium permanganate, silver oxide, gold chloride, etc., cannot be massed with the usual excipients, as they need some adhesive agent which will not cause decomposition. The most available substances are white clay (kaolin) and water, which form a plastic mass, but one requiring quick manipulation, as it soon becomes dry and crumbly. Recently, M. Carles has proposed a new excipient for pill masses of this character, namely, a mixture of 2 parts of kaolin and 1 part each of anhydrous sodium sulphate and water. Sixty grains of kaolin and 30 grains of the sodium sulphate require forty minims of water to form a plastic mass, which dries slowly and retains its plasticity for six or eight minutes; it admits of much better manipulation than clay and water alone, and the pills, when formed, soon become hard and retain their

shape, owing to the assumption of the crystallized state by the anhydrous sodium sulphate under the influence of water. When potassium permanganate is to be made into pills with this excipient, a larger quantity of water must be used; the best plan is to rub 30 grains of potassium permanganate into fine powder, mix well with 30 grains of kaolin and 15 grains of anhydrous sodium sulphate and then mass with sufficient water, usually 25 to 30 minims. A mixture of equal parts of kaolin, or Fuller's earth, soft petrolatum, and paraffin, forms a most excellent excipient for this class of pills, or the medicinal agent, in fine powder, may be incorporated with its own weight of lanolin, or wool fat, deprived of its water, and then sufficient kaolin be added to form a mass. Lanolin is indifferent toward silver nitrate and potassium permanganate (Hager). Another satisfactory method is to mix potassium permanganate with one-half or the whole of its weight of kaolin and then mass with one-fourth its weight of soft petrolatum.

When deliquescent substances, or such as slowly volatilize upon exposure to air, are ordered in pill form, a mixture of potassium borotartrate with half its weight of water will prove a good excipient; about one-sixth of a grain of powdered tragacanth should be added for each pill, and the mass must be quickly formed and rolled out; 60 grains of chloral hydrate or 30 grains of potassium iodide require 2 drops of the excipient. Even potassium acetate has been made into satisfactory pills by the aid of potassium borotartrate, 18 parts of the former and 3 parts of the latter being used with 1 part of water. All such pills must be dispensed in bottles.

The third class, absorbent excipients, are frequently required to supply the necessary firmness to a pill-mass, so that the original shape given to the pills may be retained. The addition of absorbent powders must be made judiciously, so as to avoid an unnecessary increase in the bulk of the mass, and the quantity used should be noted on the prescription, so that in case of a repetition pills of the same size may be dispensed. The reckless use of solvent as well as absorbent excipients is one of the chief errors of inexperience, and often causes much trouble. Some absorbent powders, such as starch, calcium phosphate, magnesium carbonate, liquorice root, and orris root, possess little or no adhesive properties, and, if used in excess will cause the mass to crumble; others, like marshmallow root, acacia and elm-bark, containing much mucilaginous matter, if used in excess, form hard and slowly soluble combinations.

For pill-masses containing an excessive quantity of soft, solid extracts, powdered liquorice root will be found very desirable and preferable to powdered elm-bark, unless metallic salts are present in large proportion. For volatile oils, creosote, and liquid oleoresins, soap is decidedly the best excipient, as it emulsionizes these and prevents their separation during subsequent manipulations; from one-half to one grain of soap is necessary for each minim of oil, and stearin or curd soap will be found preferable to olive-oil soap. In

the absence of any vegetable powder in the prescribed combination, the addition of powdered liquorice root is desirable, and a mixture of 1 part of soap and 5 parts of liquorice root forms a convenient excipient, of which 3 grains should be used for each minim of volatile oil; if necessary, water or diluted alcohol may be used to facilitate massing. The incompatibility of soap and soluble metallic salts in pill-masses has already been noted in a previous paragraph. For creosote, when ordered by itself, powdered liquorice root and water are very serviceable; 2 grains of the powder with a little water are sufficient for each drop of creosote. Carbolic acid can be treated like creosote, and soap will be found to bind it very nicely.

Tar, when prescribed in pill form, either alone or in connection with other remedial agents, requires the addition of an absorbent; magnesium carbonate and powdered liquorice root have been recommended, but calcium phosphate, used in twice the weight of the tar, has been more satisfactory, yielding a firm yet plastic mass. Pills thus made retain their original shape and disintegrate quite readily in water. For making pills of mercurial ointment, the same excipient has been used with success.

Hager has suggested a mixture of equal weights of yellow wax and starch, in the form of powder, as a superior adhesive and absorbent excipient for numerous troublesome pill-masses; starched wax is decidedly preferable, as an excipient, to wax with an addition of some fibrous vegetable powder, as pills made with the former disintegrate more rapidly, and the wax, being in a state of fine division, is less liable to cause intestinal trouble. From 3 to 5 grains of starched wax will yield a satisfactory mass with 1 grain of each of the following substances (Hager): Carbolic acid, apiol, oleoresin of male fern, guaiacol, creosote, croton oil, terpinol, and oil of tar. Starched wax may be prepared by thoroughly drying yellow wax, in the form of thin shavings, under paper cover in a dark place, and then rubbing into powder with an equal weight of rice-flour.

Unless some other substance is present, as an oleoresin or a volatile oil, whereby the melting-point of the mixture is brought down to about 38° C. (100.4° F.), wax is very undesirable in pill-masses on account of its difficult disintegration, which may cause pills made therewith to pass through the body unaltered. When wax is directed to be used in a pill-mass, it should be melted at a moderate heat and then mixed with any oil or oleoresin ordered, before the solid ingredients are added.

Powdered tragacanth may sometimes be employed as an absorbent when it is desired to impart adhesiveness to a very moist mass, without materially increasing the bulk. The mixture of tragacanth and powdered elm-bark previously mentioned, is, however, generally to be preferred. The compound tragacanth powder of the British Pharmacopœia, composed of 1 part each of powdered tragacanth, powdered acacia and starch, and 3 parts of powdered sugar, forms an excellent absorbent and adhesive excipient. These pills disintegrate readily.

A mixture of equal parts of finely-powdered elm bark and starch will be found a most desirable excipient for soft pill masses containing iodine or iodide of iron; the mass should be rolled out while still moderately soft, as the pills will harden subsequently. Pill-masses containing free iodine should invariably be made with the addition of starch, which, combining with the iodine, prevents its irritating effect on the mouth and throat; the union between the starch and iodine is very feeble, and the latter will be again liberated by the warm liquids of the stomach.

In a few cases the addition of any excipient is superfluous, as when lupulin and camphor are ordered together in pill form. The simple trituration of powdered camphor with lupulin causes the resinous matter to soften, and an adhesive mass is quickly obtained, which hardens again on standing. All solvents, like ether, alcohol, and diluted alcohol, must be avoided, but a very small quantity of elm bark may sometimes be added with advantage in very warm weather.

Mortars and other utensils used in making pill-masses are sometimes cleaned with great difficulty, on account of the stain imparted by certain chemicals. As a rule, plain water, cold or hot, will suffice to remove the slight remnants of a pill-mass, especially if allowed to stand in the mortar for a short while, but in some cases the addition of lye (caustic potassa or soda solution) becomes necessary to soften hard resinous deposits. The persistent odor of volatile oils is best removed with a little alcohol, after the mortar has been well washed with water. A few drops of oil of turpentine very promptly remove the peculiar odor of iodoform. Metallic stains, as a rule, are dissolved quickly by a little strong hydrochloric or nitric acid. Manganese dioxide stains disappear at once, if treated with coarsely powdered ferrous sulphate, sulphuric acid, and water, while potassium permanganate stains yield readily to a solution of oxalic acid.

Division of the Pill-mass. After the mass has been properly prepared it is transferred to a regular pill-machine or a graduated glass or porcelain tile, to be rolled out, by means of a flat piece of hard wood, into a cylinder of uniform thickness, which is then divided into the requisite number of pieces. Steel spatulas are used by many for rolling out the mass, but are not so desirable as a wooden roller, since the width of the spatula permits of covering only a small part of the mass at a time, hence irregularity in the thickness of the cylinder frequently occurs. A little pressure must be applied when rolling the pill-cylinder. Figs. 211 and 212 represent wooden pill-mass rollers, the long one with the handle having the more convenient shape.

A small number of pills may be conveniently divided on a pill-tile (Fig. 213), but, for a larger number, a pill-machine will be found preferable, particularly if the weight of the pills corresponds to the size of the grooves, for then the perfect rounding of the pills can be

readily effected by continued rolling in these grooves. Fig. 214 represents a complete pill-machine. It consists of a smooth, hard wood rolling-board encased in metal and provided with a grooved metal plate; to the roller, which is likewise made of hard wood, is attached

Fig. 211.

Wooden pill-roller.

Fig. 212.

Pill-roller.

Fig. 213.

Pill-tile, graduated.

a similar metal plate, the grooves of which correspond exactly to the grooves of the plate on the board, being adjusted to the size of pills of certain weights, as 1, 2, 3, or 5 grains. To facilitate the motion of the roller it is frequently provided with two little metal wheels on each side of the grooved plate, as may be seen in the illustration. When

Fig. 214.

the roller is in use, these bear against the metal casing of the rolling-board, and thus enable the roller to travel uniformly.

The best pill-machine is the "Cooper patent" (Fig. 215), the woodwork being of mahogany and the metallic parts of brass. This machine has two sets of reversible grooved plates, on which four different sizes of pills can be made—1, 2, 3, and 5 grains; the plates being quickly removable and adjustable. The sides of the

rolling-board are so constructed that they can be raised or lowered by means of winged screws, which allows the mass to be rolled just the thickness required for each respective size of pills, thereby insuring always the full number of perfectly round pills.

Fig. 215.

The Cooper Patent Pill-machine.

After the cylinder has been properly rolled out to the length of the desired number of pills, it is placed upon the grooved plate of the board, and divided by applying the other cutter and drawing this forward and backward with slight pressure.

When the pill-cylinder is divided on a pill-tile, and also when the pills are larger or smaller than the grooves of the machine, it becomes necessary to impart a spherical shape to the pieces, by appropriate rolling between the thumb and first and second fingers, after which the pills should be placed under a pill-finisher and completely rounded by rotary motion of the same with some pressure. It is better to move the finisher about in curvilinear figures like the figure 8, instead of giving it a constant circular motion, so that the pressure may be uniform at all points. Pill-finishers usually consist of a circular piece of hard wood, with a smooth rolling surface and a projecting margin for the purpose of confining the pills; several sizes are required to suit different sizes of pills. Fig. 216 represents a convenient pill-finisher suitable for two different sizes, as the upper and lower margins project to different lengths.

Fig. 216.

Hard-wood pill-finisher.

Pill-dusting. The pill mass, being plastic and adhesive, is apt to adhere to the slab and the fingers while being rolled out and shaped into pills. This may be prevented by the use of a fine powder, which should be strictly inert, unless otherwise directed by the physician. Among the most suitable powders are lycopodium, liquorice root and starch. The former is particularly desirable on account of its fineness and uniformity, its slight adhesiveness and its utter tastelessness. Powdered starch should be used with all white pill-masses, Bermuda arrow-root being the best for the purpose.

Only in exceptional cases is the addition of dusting-powder to the pills in the box justifiable; the pills should receive a sufficient coating of the powder under the finisher, then, if the mass has been properly made, there will be no danger of the pills adhering, hence no occasion for putting an excess of powder in the box. Magnesia and magnesium carbonate are not well suited for dusting-powders, and should, moreover, be used with due care, on account of the possible chemical effect upon the ingredients of the pills. Powdered talc (soapstone) is likewise serviceable, having the advantage of imparting a very thin, opaque and tasteless coating to the pills, without impairing their solubility in the stomach; it is particularly suited for pills of silver nitrate and the like. When asafetida or other nauseous substances are given in the form of pill, the odor may either be entirely covered or considerably modified by the use of powdered cinnamon, aromatic powder, ginger, or similar material.

PILL-COATING. The plan of coating pills with various substances, with a view of disguising the odor and taste of nauseous medicines, is by no means a novelty, having been practised over fifty years ago. At one time, the silvering or gilding of pills was of frequent occurence, but at present it is but rarely employed. Pills to be thus coated must be made firm and rolled perfectly smooth, if possible, without any dusting-powder; they should be slightly dampened with very thin mucilage of acacia and then placed in a suitable apparatus consisting of two hollow hemispheres of hard wood or horn, as shown in Fig. 217. Silver or gold foil is added, when, the apparatus having been closed, a rapid rotary motion will, in a very short time, cause the pills to take on a uniform coating of the metal; should some of the pills receive only a partial covering, more foil must be added and the rotary motion repeated. As a rule, one leaf of silver or gold will cover a dozen two-grain pills. Glycerin should not be used as an excipient for pills which are to be silver- or gold-coated, as it will lessen the brightness of the metal.

FIG. 217.

Sugar-coating is a process which is not readily applicable to the operations of the pharmacist, requiring experience and practice to insure success. It partakes of the confectioner's art, although the coating of pills with sugar requires somewhat more care, on account of the absence of starch or flour, which generally make up a part of the confectioner's coating. Sugar-coating of pills is done, on a large scale, in hemispherical copper pans made to revolve slowly within a coil of steam-pipe supplying the necessary heat for evaporation of the moisture; the pills, which should be well air-dried, are placed in the pan, and a quantity of simple syrup or of a mixture of syrup

and mucilage of acacia is poured on, the pan being kept in constant rotary motion until the pills are dry. The addition of syrup is repeated until a sufficiently thick coating has been deposited on the pills, and this can only be ascertained by experience.

Sugar-coating can be more successfully performed with a large quantity of pills than with a small number, as the deposit of sugar takes place more uniformly, and the mutual attrition of many pills insures a smooth surface. Fig. 218 represents a sugar-coating pan in use in large manufacturing establishments; as seen in the illustration, it is operated entirely by steam-power. For small operations it will be found desirable to dampen the pills with diluted

FIG. 218.

Sugar-coating machine for pills.

mucilage of acacia or egg-albumen and then rotate them in a tinned-copper or porcelain dish containing either finely bolted sugar or a mixture of acacia 1 part and sugar 5 parts, or of sugar 2 parts, sugar of milk 1 part and purified talcum 1 part. With care and practice, very fair results may be obtained, although the pills cannot be expected to look as perfect as those coated by machinery. A small apparatus has been devised in England for facilitating the sugar-coating of pills at the dispensing counter; it is shown in Fig. 219 and consists of a flat-bottomed, tinned-copper pan, with a hinged cover. The pills having been dampened as directed, may be placed in the pan with the sugar and rotated while a gentle heat is applied, which facilitates the drying of the coating; when dry, the

process can be repeated until a perfect, hard, white coating is obtained. Sugar-coated pills do not at first have the glossy appearance so familiar to all, but are dull when taken from the coater; they are then shaken with pieces of paraffin, which causes a minute film of the latter to be deposited on the sugar, and thus the desired gloss is produced.

FIG. 219.

Small sugar-coating pan.

Gelatin-coating is more readily applied than sugar-coating, but, like the latter, requires practice to insure proficiency. The chief difficulty lies in the drying of the coating after the pills have been dipped into the solution of gelatin; the pills must be kept in motion while the gelatin cools, otherwise the coating will not be uniform. Pills to be gelatin-coated must be firm, dry and free from dusting-powder; if glycerin is used as an excipient, it is apt to soften the gelatin-coating, causing the pills to stick together. For pills containing strongly odorous substances, such as asafetida, sumbul, iodoform, the valerianates, etc., gelatin-coating is decidedly inferior to sugar-coating, as the odor very soon penetrates the gelatin. The manner of coating the pills on a large scale is identical with that used for only a dozen pills, namely, the pills are impaled upon long thin needles, to the depth of about $\frac{1}{16}$ of an inch, and then immersed in a solution of gelatin kept fluid by means of a water-bath; in order to avoid contraction and cracking of the gelatin upon cooling, mucilage of acacia is usually added to the solution, and, by some, syrup also. The rapid drying, on a large scale, is effected by placing the pills, soon after they have been dipped, while still on the needles, in specially constructed drying cases connected with an exhaust fan, by means of which, air is rapidly drawn through the cases, and the moisture is thus removed.

For small operations, various devices have been suggested for drying the gelatin-coating, no one of which can be said to be the best, as pharmacists are apt to prefer that apparatus with which they have become most familiar by practice. The gelatin solution should be kept at a temperature between 72° and 82° C. (161.6° and 179.6°

F.), so that it may not be too thick when the pills are immersed, and any scum or froth forming should be carefully pushed aside before the pills are dipped. Figs. 220, 221, 222 and 223 represent the four leading styles of gelatin-coating apparatus in use among pharmacists in this country. In three of them the pills are taken up on the needles from a tray provided with grooves, in which the pills have been placed, and, after they have been dipped into the gelatin solution, are revolved until dry and then stripped from the needles by means of a comb, shown in the illustrations. The arrangement of Prof. Patch for drying the coating, consists of a wheel with slots, in which the bars carrying the needles are placed, when the wheel is made to move alternately in opposite directions, by means of a string attached to the axle passing through the wheel (see Fig. 220). The gelatin solution recommended by Prof. Patch is made as follows:

FIG. 220.

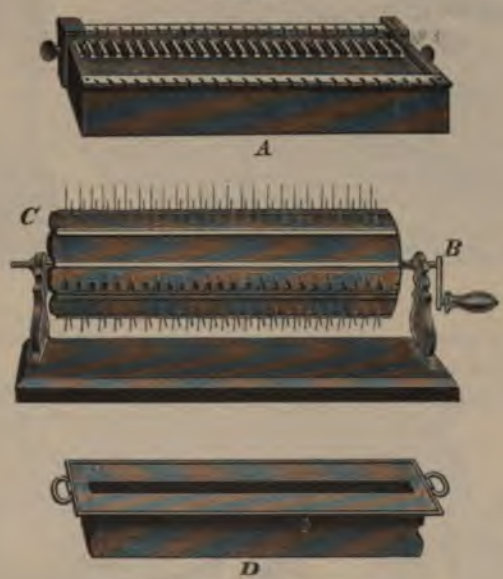
Prof. Patch's gelatin-coater.

Macerate 2½ ounces (av.) of French gelatin (gold label) with 7 fluid-ounces of distilled water, and, when soft, dissolve by aid of a hot water bath; add 2 drachms of boric acid and finally 2 fluidounces of mucilage of acacia; strain the mixture.

The "Porcupine" gelatin-coater (Fig. 221), designed by C. C. Wells, consists of a wooden tray, *A*, provided with grooves and a gauge for regulating the depth to which the needles shall enter pills of different sizes, and also a brass comb for disengaging the pills from the needles; a drying cylinder, *B*, provided with T-shaped rails on its rounded cylinder, which form grooves for receiving the needle-bars, *C*; a water-bath and solution holder, *D*, the latter being a trough in the cover of the bath and kept at the right temperature by

the aid of heat. After the needle-bars carrying pills have been placed in the grooves of the cylinder the latter is kept revolving, by means of the crank on the side (larger machines are operated by

FIG. 221.

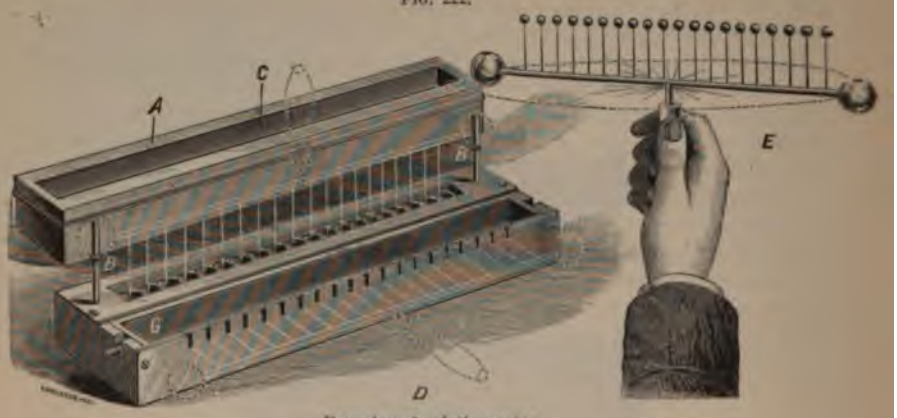


Wells' "Porcupine" gelatin-coater.

clock-work attachments), at the rate of about 50 revolutions a minute, until the pills are dry enough not to stick together when taken off the needles. Wells recommends the following solution for gelatin-coating: Dissolve 2 drachms of acacia in 1 fluidounce of water and add 1 ounce (av.) of Cox's gelatin, 2 fluidounces of water and 1 fluidounce of simple syrup; dissolve by heat and strain.

The gelatin-coater of W. C. Franciscus (Fig 222), resembles the other two, except in the provision for drying the coating on the pills, which must be done by rapidly twirling the needle-bars centred on a pivot, with the hand, until the pills are sufficiently dry to be removed. The different steps of the operation are shown in the illustration; *A* represents a water-bath, and *C* the solution-holder resting in the same; *B B* shows the position of the needle-bar in the act of impaling the pills which have been placed in the depressions in the tray, the balls on the ends of the bar insuring accuracy in centring the pills with the needle-points, by slipping over the rods *B* and *B*. At *E* is shown the manner of revolving the pills, after they have been dipped, by means of the pivotal handle, *D*. When sufficiently dry, the pills are stripped from the needles by means of the comb attached to the tray, *G*.

FIG. 222.



Franciscus' gelatin-coater.

Maynard's gelatin-coater (Fig. 223) is not provided with a grooved tray from which the pills are taken up, but, instead, the pills are placed in depressions in a metallic plate, E, provided also with two

FIG. 223.

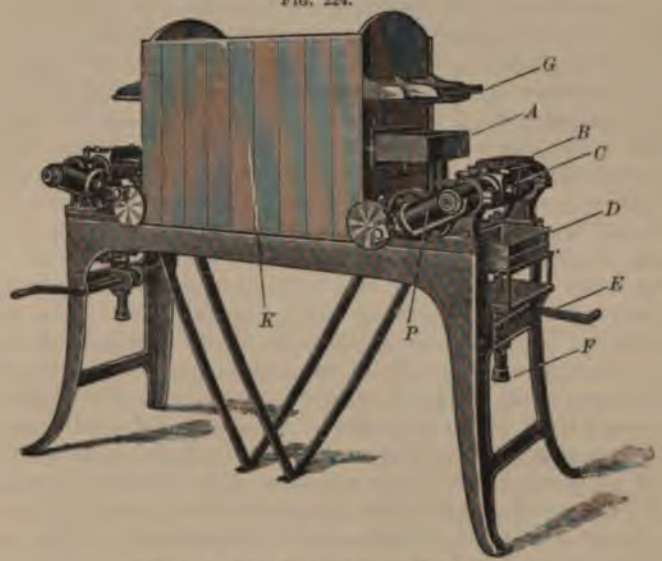
Maynard's gelatin-coater.

holes to receive the guide-pins attached to the circular needle-holder, D, and surrounded with a metallic ring, F, to keep the pills from rolling off. When the needle-holder is not in use, the needle-points are drawn back behind the outer disk by means of the handle attached to the top, to which the needles are fastened. To impale the pills, the needles are depressed, passing through the perforations in the outer disk, and take up the pills as shown at C. The gelatin solution is contained in a covered agate-ware dish, resting in the copper water-bath, A; after the pills have been dipped, the needle-holder is slowly revolved to facilitate the uniform distribution of the

gelatin film. When the gelatin has set, the needle-holder may be laid aside, as shown at C, until the coating is sufficiently hard to allow the pills to be removed to the tray of wire gauze, B, by grasping the circular plate on the needle-holder with one hand and pulling the handle upward with the other. It is always well to slightly grease the perforated disk, through which the needles pass, with petrolatum, to prevent the pills from adhering.

The application of a continuous coating of gelatin to pills without the use of needles is in successful operation at several large manufacturing establishments, but is not available at the dispensing counter, since extensive steam-power machinery is necessary for the work. In Fig. 224 may be seen a cut of probably the only machine of its

FIG. 224.



Colton's machine for continuous gelatin-coating.

kind at the present time; it was designed by Arthur Colton, of Detroit, Michigan, and has a capacity of coating from 6000 to 10,000 pills per hour. This ingeniously constructed piece of machinery is operated by two female attendants in the following manner: The pills to be coated are placed in the drawer *A*, which is provided with a perforated plate in the bottom at the end projecting from the drying-kiln. The drawer *A* having been drawn out and so arranged that the perforated plate registers over a set of tubes on plate *B*, the pills are brushed through the perforations by means of a brush moving forward and backward in *A*, and are firmly held on the tubes by a vacuum, produced by means of the pump, *P*. The tube-plate, *B*, is fastened by means of a clamp to the hood, *C*, and by revolving the latter half way the plate is brought face downward over the pan,

D, containing the gelatin solution. By means of the handle, *E*, the pan, *D*, is then slowly raised far enough to immerse the pills half way, which is regulated by the stop, *F*, so as to avoid getting any gelatin solution on the tube-plate. The plate, *B*, with the pills, is next raised and carefully placed in the slide, *G*, and another tube-plate filled with pills as before, the operation of placing the pills on the tubes and coating them being continued until the supply is exhausted. As one plate after another is placed in *G* they are pushed forward through the kiln, where the coating is dried by currents of warm air sufficiently to allow the pills to be transferred to another plate at the other end, when the operation of dipping the other half of the pills is performed by the second attendant, and the plate now carrying the completely-coated pills is returned through the kiln on a second slide running parallel to the first. When the pills again reach the first operator they are dry enough to be placed into trays.

In place of gelatin-coating at the dispensing counter, the plan prevails, in this country, of disguising the disagreeable odor and taste of pills by enclosing them in gelatin capsules. These gelatin capsules are sold under the name of *empty capsules*, and consist of small cylinders closed at one end and provided with a shorter cylindrical cover; they occur in seven sizes, ranging from ⅜ inch to 1 inch in length, and are numbered respectively from No. 5 to No. 00; they are sold at fabulously low prices. The composition of the empty capsules made in this country is a mixture of gelatin and glycerin in variable proportions, dependent upon the character of the gelatin. The French Pharmacopœia recommends for hard capsules a mixture of 30 parts each of white gelatin, gum arabic, and sugar, 10 parts of clarified honey, and 100 parts of water, to be melted with the aid of a water-bath; for elastic capsules is recommended a mixture of 50 parts of white gelatin, 15 parts each of gum arabic and sugar, 12½ parts of glycerin, and 80 parts of water, to be likewise dissolved on a water-bath. Other authorities propose for hard capsules a mixture of 60 parts of gelatin, 10 parts each of acacia and sugar, and 50 parts of water; and for soft capsules a mixture of 50 parts of gelatin, 16 parts of sugar, 20 parts of glycerin, and 90 parts of water.

The capsules are made by dipping either metallic, bone, or wooden moulds, attached by means of handles to a suitable disk, into the melted gelatin mass kept at a temperature of about 40° C. (104° F.), and then rotating the moulds gently for a few minutes so as to insure a uniform film; if necessary, the immersion is repeated. To prevent adhesion of the gelatin solution to the moulds, the latter are rubbed with a soft oiled cloth before dipping them. After twenty or thirty minutes the gelatin film will have become sufficiently firm to allow the capsules to be stripped from the mould, and laid aside to dry in suitable closets provided with a draft of moderately warm air, any excess of gelatin being removed with an ivory knife before the capsule is taken from the mould.

As the object of capsuling pill-masses is to render the medicine

as palatable as possible, care should be taken that the exterior of the capsule be not contaminated in any way with the material. This is best accomplished by dividing the mass into small cylindrical pieces, rounding off the ends of each, and then, after having washed the hands thoroughly, introducing the pieces, by the aid of a long needle, into the capsule held in the left hand, taking up the cover with two fingers of the right hand holding the needle and quickly slipping it into position, thus avoiding all contact of the mass with the exterior of the capsule. The habit of putting pills into capsules with the fingers is censurable and an evidence of bad training.

The filling of capsules with liquids is, as a rule, done in large manufactories, and, for this purpose, capsules of ovoid shape having a small orifice are selected; they are supported on trays or racks, and the liquid is introduced by means of a pipette or a syringe with a small nozzle. The orifice of the capsule is finally closed by putting over it a little of the warm gelatin solution, with a glass rod. When the pharmacist has occasion to dispense liquids in ordinary empty capsules the best plan is to set the capsules up in a shallow box with a perforated lid, and, having introduced the liquid, seal the cover hermetically by moistening the edges in a drop of water spread on a pill-tile, before slipping it over the capsule; a mere trace of water being sufficient to cause a union between the cover and the capsule, any excess of moisture must be shaken off, as it would cause the capsule to soften and finally leak.

The well-known French pearls of ether, apiol, chloroform, etc., are gelatin globules filled with the respective liquids. According to Thévenot, they are prepared as follows: A mass composed of gelatin, acacia, sugar, and honey, is rolled out into thin sheets, one of which, while still soft, is placed upon an iron plate of 6 millimeters (about $\frac{1}{4}$ inch) thickness, and containing numerous suitable cavities of 10 millimeters (about $\frac{2}{5}$ inch) diameter, into which the mass sinks by reason of its own gravity, thus forming a hollow hemisphere in each cavity; the desired liquid is introduced by means of a pipette or small syringe, and a cover consisting of another sheet of the same gelatin mass is laid on. A second iron plate corresponding exactly to the one first used, is now placed over the last sheet, and, after screwing the plates together their position is reversed so that the second gelatin sheet may fill the cavities in the second iron plate, thus completing the spherical shape of the pearls or globules, which are finally separated from each other by subjecting the whole arrangement to powerful pressure.

Another method is said to consist in filling a tube, made of gelatin composition, with the respective liquids, and then, by means of a specially constructed machine, cutting off pieces of the required size and simultaneously pressing these into the proper shape. The apparatus used for this method was invented by a French pharmacist and is known as Viel's Capsulator.

Pills are sometimes coated with collodion or balsam of tolu; the

latter plan is directed in the official formulas for pills of iodide of iron and of phosphorus. To coat pills with collodion, they are simply impaled on needles and dipped into collodion, which is then allowed to dry; if water be present in the pills, the coating will become mottled or opaque. The Pharmacopœia directs a solution of 10 Gm. of balsam of tolu in 15 Cc. of ether, for coating pills, but, owing to the very rapid evaporation of the solvent, the process is very unsatisfactory, as the pills are apt to stick. A better plan is to follow the suggestion of Prof. Patch, which is as follows: Dissolve 540 grains of balsam of tolu and 180 grains of mastic in 2 fluid-ounces of alcohol, and filter through cotton. Coat the interior of two flat evaporating dishes with a very thin film of oil of sweet almond or petrolatum, place the pills to be coated in one of the dishes, add a few drops of the solution, cover with the second dish and rotate rapidly until the pills are well coated, then put on a tray to dry.

The so-called "pearl coating" is applied in a manner similar to that used for gilding or silvering; the pills having been evenly dampened with a very thin adhesive liquid (mucilage of acacia ʒj, syrup ʒj, and water ʒvj, or tragacanth 4 grains, syrup ʒss, and water ʒvijss), are rotated in a globular box with purified talcum or a mixture of talcum and sugar in the form of an impalpable powder. If a high polish is desired, this can be obtained by rotating them afterward in another globe coated on the inside with paraffin.

Keratin coating has been especially recommended for pills which are not to be acted upon in the stomach, but to be soluble in the intestinal fluids. Keratinized pills were first introduced by Dr. Unna, of Germany, but have not met with much favor, on account of the tedious process of coating. Keratin is a constituent of all horny matter and is obtained from the same, after removal of fat with ether, by digestion in the form of shavings or turnings, with a mixture of pepsin, hydrochloric acid, and water, for twenty-four or thirty-six hours; this treatment removes all matter soluble in the gastric juice. The residue, having been well washed with water, is digested with eight or ten times its weight of 5 per cent. ammonia water in a loosely stoppered flask, at a moderate heat, until a nearly complete solution results, which is then filtered and evaporated to dryness. Keratin, as thus prepared, is a commercial article; both acid and alkaline solutions of it are used for coating pills.

Ammoniacal solution of keratin is prepared by dissolving 7 parts of keratin in a mixture of 50 parts of 10 per cent. ammonia water and 50 parts of 60 per cent. alcohol (solution may be facilitated by warming). This alkaline solution should be used for pills containing trypsin, pancreatin, metallic sulphides, etc.

Acetic solution of keratin, made by dissolving 7 parts of keratin in 100 parts of glacial acetic acid (if necessary, by the aid of a moderate heat), is adapted for pills containing ferric chloride, tannin, salicylic acid, arsenic, creosote, and the salts of mercury, gold, and silver.

For chemically indifferent substances, either the alkaline or acid solution of keratin may be employed.

All pills intended to be coated with keratin must be made with some fatty excipient and contain no appreciable moisture; the mass is best made with cacao-butter and oil of sweet almond, or a mixture of purified mutton-tallow or cacao-butter 10 parts and white or yellow wax 1 part. After the pills have been rounded they should be dipped in melted cacao-butter, which is allowed to harden; they are then placed in a porcelain dish, the keratin solution added (about 30 or 40 drops for 100 pills of medium size) and rotated until the pills have become thoroughly moistened, after which they are dried on parchment paper, to which they will not adhere. The application of keratin solution must be repeated three or four times and allowed to dry each time.

To avoid the tediousness of coating with keratin, salol coating has been recommended, which is best applied by melting salol in a dish and dipping the pills, fixed on needles, into it, afterward closing the small needle-holes separately. Salol, like keratin, is insoluble in the gastric juice, but the coating has not been found so satisfactory.

The Official Pills.

The U. S. Pharmacopœia gives working formulas for 15 varieties of pill-masses, and as these are directed to be divided into a definite number of pills, they are indicated under the title "Pilulæ." The term "Massa" is applied to those combinations which are intended to be kept on hand in bulk, being frequently prescribed as constituents of other pill-masses. In the British Pharmacopœia 21 formulas for pill-masses are given, but in no case is the mass directed to be divided into a given number of parts; they are all designated by the simple title "Pilula."

ALPHABETICAL LIST OF THE OFFICIAL PILLS.

Name.	Composition of each Pill.		Excipient.
Pilulæ: Aloes	Purified Aloes	0.13 Gm.	Water.
	Soap	0.13 "	
Aloes et Asafœtidæ	Purified Aloes	0.09 Gm.	Water.
	Asafetida	0.09 "	
	Soap	0.09 "	
Aloes et Ferri	Purified Aloes	0.07 Gm.	Confection of Rose.
	Dried Sulphate of Iron	0.07 "	
	Aromatic Powder	0.07 "	
Aloes et Mastiches	Purified Aloes	0.13 Gm.	Water.
	Mastic	0.04 "	
	Red Rose	0.03 "	
Aloes et Myrrhæ	Purified Aloes	0.13 Gm.	Syrup.
	Myrrh	0.06 "	
	Aromatic Powder	0.04 "	

Name.	Composition of each Pill.		Excipient.
Pilulæ: Antimonii Compositæ	Sulphurated Antimony	0.04 Gm.	Castor Oil.
	Mild Mercurous Chloride	0.04 "	
	Guaiac	0.08 "	
Asafœtidæ	Asafetida	0.20 Gm.	Water.
	Soap	0.06 "	
Catharticæ Compositæ	Comp'd Extract of Colocynth	0.08 Gm.	Water.
	Mild Mercurous Chloride	0.06 "	
	Extract of Jalap	0.03 "	
	Gamboge	0.015 "	
Catharticæ Vegetabiles	Comp'd Extract of Colocynth	0.06 Gm.	Water
	Extract of Hyoscyamus	0.03 "	
	" " Jalap	0.03 "	
	" " Leptandra	0.015 "	
	Resin of Podophyllum	0.015 "	
	Oil of Peppermint	0.008 Cc.	
Ferri Carbonatis	Ferrous Sulphate, crystallized	0.16 Gm.	Glycerin and Water.
	Potassium Carbonate	0.08 "	
	Sugar	0.04 "	
	Tragacanth	0.01 "	
	Althæa	0.01 "	
Ferri Iodidi	Reduced Iron	0.04 Gm.	Water.
	Iodine	0.05 "	
	Glycyrrhiza	0.04 "	
	Sugar	0.04 "	
	Extract of Glycyrrhiza	0 01 "	
	Acacia	0.01 "	
Opii	Powdered Opium	0 065 Gm.	Water.
	Soap	0.02 "	
Phosphori	Phosphorus	0.0006 Gm.	Glycerin and Water.
	Althæa	0.060 "	
	Acacia	0.060 "	
Rhei	Rhubarb	0.20 Gm.	Water.
	Soap	0.06 "	
Rhei Compositæ	Rhubarb	0.13 Gm.	Water.
	Purified Aloes	0.10 "	
	Myrrh	0.06 "	
	Oil of Peppermint	0 005 Cc.	

Special Remarks.

If it is desired to keep any of the official pills in stock in an uncoated condition, they should at once be placed in a mixture of lycopodium and powdered liquorice root and allowed to remain there until dry, which may require from four to eight days; they can then be kept in bottles, without danger of moulding or losing their shape. This plan is particularly advisable for the Compound and Vegetable Cathartic Pills.

Pilulæ Aloes et Asafœtidæ. Select tears of asafetida only should be used, and it will be found advantageous to make a plastic mass of the gum-resin and soap with a *small quantity of water*, and then incorporate the powdered aloes. Excess of moisture must be carefully guarded against.

Pilulæ Aloes et Mastiches. These pills, commonly known as Lady

Webster Dinner Pills, are apt to become very hard in time, hence it appears preferable either to make them up fresh when wanted or to use a mixture of syrup and water, equal parts, or glycerin and water, equal parts, in place of water as an excipient. The mastic must be used in fine powder, and the three powders should be well mixed before any excipient is added.

Pilulæ Antimonii Compositæ. These pills were at one time extensively prescribed under the name of *Plummer's Alterative Pills*, and prescriptions calling for 100 pills at a time were not unusual. The use of castor oil as an excipient in place of mucilage of tragacanth is a decided improvement, and was taken from the British Pharmacopœia. A little care is necessary to avoid an excess of oil, which renders the pills soft and greasy. After the powders have been well mixed, the castor oil should be added, a few drops at a time, and the mixture well kneaded after each addition, until a firm mass is obtained which is not greasy to the touch. It must be borne in mind that the oil acts as a solvent upon the resin, which, thus becoming soft, can be readily combined into a mass with the metallic powders. The stain left in the mortar when making Plummer's Pills is best removed with soap and water (preferably hot), followed by hydrochloric acid.

Pilulæ Catharticæ Compositæ. In making these well-known pills, powdered extract of jalap is to be preferred to the pilular extract officially directed; it should be first mixed with the gamboge and calomel and finally with the powdered compound extract of colocynth. A moderate quantity of water (fl℥vi for 1000 pills), which should be added to the powders all at once, suffices to make a satisfactory, firm mass, provided the mixture be well kneaded in the mortar. Compound Cathartic Pills should never be put away in stock bottles until perfectly dry and hard.

Pilulæ Ferri Carbonatis. — Blaud's pills, as the official pills of ferrous carbonate are more commonly termed, have probably caused inexperienced pharmacists more trouble than any other pill-mass; this is partly owing to the fact that physicians frequently order equal parts of ferrous sulphate and potassium carbonate, which renders the mass very deliquescent, on account of the excess of potassium carbonate. The official formula yields very satisfactory results, the secret of success lying in the completed reaction between the iron and potassium salts, before the final massing with tragacanth and althæa. The mass should be rolled out and cut while still moderately soft. The official formula is based on the assumption that absolutely pure potassium carbonate will be used, in which case the decomposition will be complete, as the 16 Gm. of crystallized ferrous sulphate require 7.954 Gm. of potassium carbonate, yielding 6.673 Gm. of ferrous carbonate; if the potassium carbonate used be less than 100 per cent. pure, an excess of ferrous sulphate will be present.

Physicians are in the habit of prescribing four drachms each of ferrous sulphate and potassium carbonate to be made into 100 pills,

which proportions should be changed to 4 drachms and 140 grains respectively. The following method of procedure, which I have used with marked success for many years, was, I think, first suggested by Mr. Tscheppe, of New York: Rub the 240 grains of crystallized ferrous sulphate into a fine powder with 30 grains of sugar, and mix with 140 grains of potassium carbonate also reduced to powder; the mixture, which will soon soften and change color, should be stirred from time to time until the reaction is complete, which is known by the disappearance of the granular condition and the formation of a green, smooth, very soft paste. Now add 30 grains each of powdered starch and powdered acacia, mass quickly, and roll out while still soft, as the mass rapidly becomes firm and may then crumble when rolled out.

Blaud's pills are intended to contain about 0.0667 Gm. (about 1 grain) of ferrous carbonate, and cannot be kept on hand uncoated on account of the tendency to rapid oxidation of the iron salt, which is retarded, but not entirely obviated, by the sugar or sugar and glycerin present. The pills should be of a uniform deep green color, and are best prepared fresh when wanted. In Great Britain, the mass for Blaud's pills is officially recognized by the simple term "Pilula Ferri," and its composition is about the same as that published in our own Pharmacopœia.

Pilulæ Ferri Iodidi. The official pills of ferrous iodide are presumably identical with Blancard's Pills; they contain an excess of iron, which aids in their preservation. Each pill is designed to contain about 0.0610 Gm. (about 1 grain) of ferrous iodide. Owing to the heat generated by the union of the iodine with the finely-divided iron, the former should be added slowly, so as to avoid loss by vaporization, and the mixed powder should not be added until all traces of free iodine have disappeared. When the mass has been evaporated to a proper consistence on a water-bath it will weigh about 20 Gm. The 5 Gm. of iodine ordered in the official formula require 1.104 Gm. of absolutely pure iron to form ferrous iodide; the amount of iron in excess will, therefore, depend upon the purity of the reduced iron used.

Since pills of ferrous iodide are not, as a rule, made extemporaneously, and are readily affected by air and moisture, the Pharmacopœia very properly directs a resinous coating to be applied; the advantage of a solution of balsam of tolu and mastic in alcohol over an ethereal solution of balsam of tolu has already been referred to on page 328.

Pilulæ Phosphori. The uniform distribution of phosphorus in a pill-mass is best effected in a state of solution, and the choice of chloroform as a solvent in the official formula has a double advantage. Chloroform, besides being one of the best solvents for phosphorus known, is readily dissipated, owing to its very volatile nature, leaving the phosphorus, in a very finely divided form, intimately distributed throughout the mixed powders, whilst its heavy, non-inflammable

vapor hovers over the mortar during the making of the pill-mass, thus protecting the phosphorus against oxidation. Phosphorus, being very inflammable, must be cut and weighed under water, hence the weighing of small quantities is often attended with much difficulty. A small glass capsule, or a watch-crystal, containing some water, should be carefully tared, and in it the phosphorus, having been cut into small pieces under water with a penknife, should be weighed; the pieces may be removed with a small pair of forceps, quickly dried by means of filtering paper, and then dropped into the chloroform contained in a test-tube.

Phosphorus is rapidly oxidized, particularly in a state of fine division, hence pills of phosphorus should be coated as soon after they have been made as possible; as in the case of pills of ferrous iodide, the alcoholic solution of mastic and balsam of tolu is preferable to the official ethereal solution.

Each pill contains 0.0006 Gm. (practically $\frac{1}{100}$ grain) of phosphorus.

Pilulæ Rhei Compositæ. Compound pills of rhubarb will become very hard by age, and as they are not often called for, it is decidedly better to keep the ingredients properly mixed, in a glass-stoppered bottle, and make the mass when required. A mixture of syrup and water, or glycerin and water, may be used with advantage in place of water, as in the case of pills of aloes and mastic.

The Official Masses.

As stated before, these masses are usually employed as constituents of other pill-masses; they are Massa Copaibæ, Massa Ferri Carbonatis, and Massa Hydrargyri. The last named alone is of sufficiently firm consistence to admit of being rolled into pills which will retain their spherical shape without the addition of absorbents, except when freshly made in warm weather.

Mass of Copaiba. This is made by mixing six parts of calcined magnesia, previously dampened with water, with ninety-four parts of copaiba, heating the mixture for one-half hour on a water-bath, and setting it aside until it has assumed a pilular consistence. Copaiba contains an acid resin capable of uniting with magnesia to form a solid mass, which may be looked upon as magnesium copaivate; upon exposure this resin compound becomes dry and hard. Of the different commercial varieties, the Maracaibo copaiba is best adapted for making the official mass; it is thicker than the rest, not quite transparent, and contains less volatile oil. When mixed with $\frac{1}{16}$ of its weight of freshly-calcined magnesia, good Maracaibo copaiba becomes heated and sets to a solid mass in the course of a few hours. Experience has taught that the previous addition of water to the magnesia materially facilitates the reaction. Mass of copaiba is sometimes known as solidified copaiba; although it can be formed into pills, these will not retain their shape unless some vegetable powder has been added.

Mass of Ferrous Carbonate, or Vallett's Mass, is a mixture of ferrous carbonate, sugar and honey. Even when very carefully made, so as to contain the full amount of iron salt, it is never of a pilular consistence, but always in the form of a rather tenacious paste. The Pharmacopœia directs the formation of ferrous carbonate by mixing solutions of ferrous sulphate and sodium carbonate in the presence of sugar, and then washing the precipitate well with sweetened water until the newly-formed sodium sulphate has been removed; the washing is best performed by decantation in flasks having a narrow neck, and which can be tightly stoppered. Theoretically the official product should contain about 42 per cent. of ferrous carbonate, as 100 Gm. of crystallized ferrous sulphate will yield 42 Gm. of the carbonate, but as there is always some loss during the washing process, the finished mass rarely contains more than 36 per cent., and this much only, if care has been observed to prevent oxidation by rigid exclusion of air. Freshly precipitated ferrous carbonate is greenish-gray, gradually deepening in color, and the finished mass is decidedly green, but should not be brown, which would indicate oxidation. When Vallett's mass is allowed to stand for some time, even in well-covered jars, it becomes dry on the surface, and assumes a blackish-green color. The change extends to the interior very slowly, being due to the gradual escape of moisture.

Mass of Mercury, better known as Blue Mass or Blue Pill, is probably the most familiar of all pill-masses. In the official formula thirty-three parts of mercury are triturated with a mixture of three parts of glycerin and thirty-four parts of honey-of-rose, until extinguished, the viscid character of the vehicle enabling a rapid division into minute globules. When mercury is no longer visible to the naked eye, and the mixture has assumed a uniform brownish-gray appearance, five parts of powdered liquorice-root and twenty-five parts of powdered althæa are gradually added with constant trituration, until the mercury is so finely divided that it cannot be detected with a lens of at least ten diameters magnifying power. Blue mass contains 33 per cent. of metallic mercury, which probably undergoes slight superficial oxidation in the course of time, but is well protected by the other ingredients. In my experience the mass will be somewhat improved in consistence if the amount of glycyrrhiza officially directed be doubled and the amount of althæa correspondingly decreased.

CHAPTER XXIX.

CONFECTIONS AND LOZENGES.

Confections.

THIS now almost obsolete class of medicinal preparations still finds recognition in the leading pharmacopœias, although, in this country, at least, they are very rarely used by physicians. At one time the incorporation of saline and vegetable remedial agents with honey or fruit-pulp was a favorite mode of medication, such being the invariable composition of electuaries or confections which were dispensed in the form of a thick semifluid mass. When made with honey, or with the addition of glycerin, confections will retain their original soft condition for a long time; but if made with fruit-pulp, or sugar and water, the moisture gradually evaporates and the mass becomes dry and hard. All medicinal ingredients must be added in the form of impalpable powder, and heavy metallic salts should never be employed, as they are apt to sink to the bottom, and thus become separated. Whenever essential oils are to be incorporated in confections they should first be triturated thoroughly with some finely-powdered sugar; narcotic extracts or other potent remedies should be added in the form of solution, so as to insure their uniform distribution throughout the soft mass.

The U. S. Pharmacopœia at present recognizes but two confections, and the German Pharmacopœia one (*Electuarium Sennæ*), while the British Pharmacopœia still retains eight—namely, *confection of hips, opium, pepper, roses, scammony, senna, sulphur*, and *turpentine*.

The Official Confections.

Confectio Rosæ. This preparation, which at one time was largely used as a favorite excipient for certain pill masses, possesses little or no medicinal virtue. It contains 8 per cent. of red rose leaves, which are rubbed with warm rose-water previous to the mixture with sugar and honey, for the purpose of reducing the rose petals to the condition of a soft pulp, and thus replacing freshly gathered rosebuds.

Confectio Sennæ. Confection of senna, sometimes called for under the name of lenitive electuary, if carefully prepared, presents an agreeable mild laxative preparation. If the fig, tamarind, prune, and purging cassia, finely bruised, be digested with the water, in a covered vessel, for three hours, on a boiling water-bath, and occasionally stirred with a stiff glass-rod or porcelain spatula, there will be no necessity to rub the pulp through a coarse hair-sieve with the

hands, since a horn or porcelain spatula will answer as well, and is surely more desirable in every way. After the sugar has been dissolved in the hot pulpy liquid, the mixture evaporated to the required weight and allowed to cool somewhat, the senna and oil of coriander, having previously been triturated with a portion of the sugar, may be incorporated.

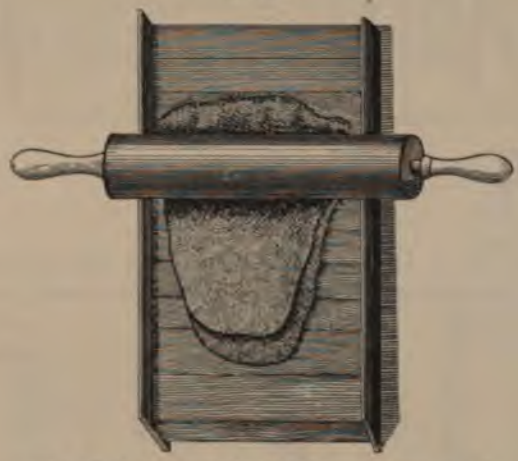
Lozenges or Troches.

Lozenges are solid, flattened masses of round, oval, or other desirable shape, not intended for mastication, but to be dissolved slowly in the mouth, therefore, not adapted for medicines which are expected to undergo disintegration in the stomach prior to any therapeutic action. In one or two cases the cylindrical form is preferred, as for the well-known liquorice lozenges and Wistar's cough lozenges. The remedial action of lozenges is generally designed to be purely local, either as an expectorant, demulcent, stimulant, sedative, astringent, or antiseptic.

The usual base or vehicle for lozenges is sugar (that known among confectioners as lozenge sugar being preferred), although powdered extract of liquorice is also added at times, and, of late years, fruit paste, made from black or red currants, has been advocated for certain kinds of lozenges. Adhesiveness is obtained by the addition of tragacanth or acacia, and syrup or water (plain or aromatic) is used to supply the necessary moisture. All medicinal constituents, as well as the sugar or extract of liquorice, should be in very fine powder to insure a smooth paste, and potent remedies, wherever possible, should be added either in the form of solution or triturated with a small quantity of sugar before being mixed with the other ingredients, so as to insure uniform distribution. Tragacanth is preferable to acacia for making a lozenge mass, as the resulting paste is more tenacious; in both cases the mucilage is to be preferred to the powder with the subsequent addition of water, as, in the latter case, it is often difficult to avoid an excess of moisture, which retards subsequent drying. Lozenge-masses are made after the manner of pill-masses, except that more adhesive material is used, and the paste is made somewhat softer. The proportion of powdered tragacanth necessary for a well-made plastic mass may vary from 1 to 3 per cent. of the total weight of the mixed powders (acacia about three or four times as much); and, in making the mass, the necessary water or syrup should be added cautiously, and the mixture well kneaded after each addition, so as to avoid too soft a condition, which readily occurs on account of the great solubility of the sugar. A good plan is to follow the suggestion of Hager, to reserve about one-fifth of the powder, and, when the remaining four-fifths have been made into a plastic mass, quickly incorporate the reserve portion, which can be done without risk of the mass becoming dry or crumbly. For massing small quantities of material a Wedgewood mortar and pestle will be found quite convenient, while for large quantities the pill-mass mixers shown on page 310 are preferable.

After a suitable mass has been made it is transferred to a hard-wood board or a stone slab, rolled out into either a flat sheet or a cylinder, and divided into the requisite number of parts. When cylindrical lozenges are to be made, the mass is rolled out without dusting and divided into pieces about five-eighths of an inch in length, by means of a special cutter. In order to prevent the mass from adhering, the flat roller may be lightly rubbed with a very small quantity of oil of sweet almond. For flat lozenges the mass is conveniently rolled out into a sheet, the required thickness of which must be ascertained by experiment; this is done by dividing the weight of the whole mass by the number of lozenges to be made, then weighing off as many grains of the mass as correspond to the quotient obtained, and forming this into a lozenge by means of a punch or spatula. As every well-made lozenge-board is provided

FIG. 225.



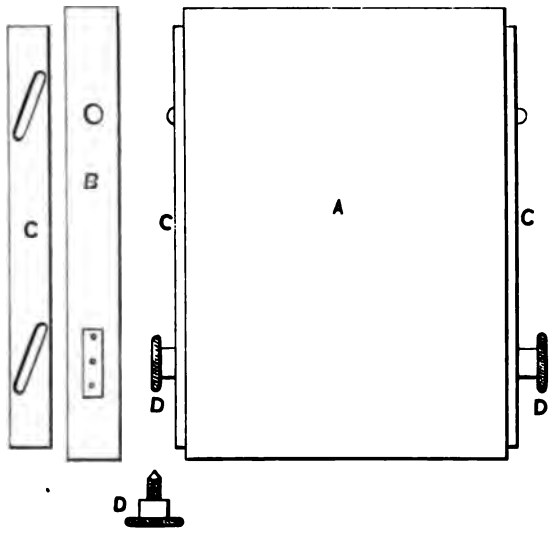
Showing the manner of rolling out the lozenge-mass.

with guides and screws for regulating different thicknesses, no difficulty will be experienced in adjusting the side strips to the proper height, and then rolling out the mass by means of a cylindrical roller, as shown in Fig. 225. To prevent adhesion of the mass, the board may be dusted with a little starch or a mixture of starch and sugar.

The lozenge-board lately designed by Wallace Procter is very useful and simple in construction, as shown in Fig. 226. A is a board of well-seasoned hard wood, $1\frac{1}{2}$ inches thick, 10 inches wide, and 14 inches long, planed perfectly flat, and both sides and ends made square and true. At each side, about 3 inches from one end, a plate is let in flush and tapped with a screw, as shown in B. On each side of the board a plate of brass, $1\frac{1}{2}$ inches wide, 14 inches long, and $\frac{3}{16}$ of an inch thick, is fitted. Each plate has two slots crossing

it diagonally (see C) $\frac{3}{8}$ of an inch from each edge; these slots must have exactly the same slope, and the front slot should be ruled to

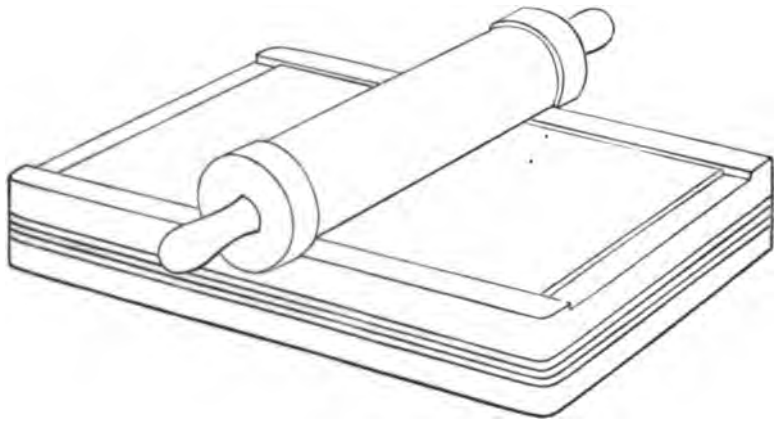
FIG. 226.



Procter's lozenge-board.

divisions of $\frac{1}{32}$ of an inch. Through one slot of each plate a square-shouldered screw passes, and is screwed in until it presses the

FIG. 227.



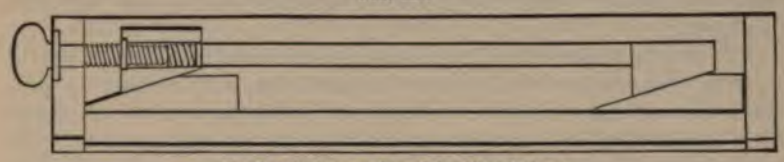
Harrison's lozenge-board.

plate close to the side of the board, but still permits it to move easily; through the other slot in each plate passes a set screw, which

enters the screw-plate before mentioned. When the plates have been adjusted to a given height the set screws are turned until they prevent motion of the plate.

Harrison's lozenge-board (see Fig. 227), which has been known for some years, consists of two frames of wood, of which one moves

FIG. 228.



Harrison's lozenge-board (sectional view).

forward and backward inside of the other in grooves cut into the outer frame; the board on which the mass is rolled rests firmly on the inner frame, and has fastened to its bottom two bevelled strips corresponding to similar strips attached to the frame. By means of

FIG. 229.

Plain tin lozenge-cutter.

FIG. 230.

Tin lozenge-punch with steel cutter.

FIG. 231.

Lozenge-punch with spring.

a screw the inner frame can be pushed forward, and the board thus forced upward (see Fig. 228). As the bevels give $\frac{3}{8}$ of an inch rise, for which fifteen complete revolutions of the screw are required, each

half-turn of the screw will cause a rise of $\frac{1}{80}$ of an inch; in this way any required thickness of the mass can be obtained. The outer frame is stationary, the sides projecting $\frac{3}{8}$ of an inch above the ends, and serving as a support for the rolling-pin, which is also provided with a flange at each end to keep it in proper position. While the rolling-pins are usually made of wood, steel or glass rollers may also be used, the former being particularly desirable when heat is to be employed.

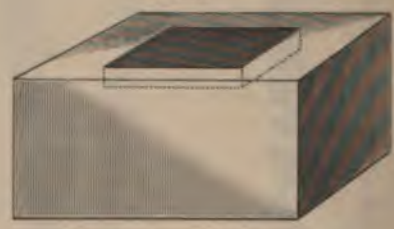
The punches used for cutting lozenges are usually in the form of tapering cylinders made of heavy tinned-iron, and frequently provided with sharp cutters of hardened steel, the shape of which varies with the fancy of the operator; sometimes they are made with straight sides and fitted with a plunger, operated by a spring, for the ready expulsion of the lozenges. Figs. 229, 230, 231 represent some of the usual styles. In large manufacturing establishments ten or twelve cutters are frequently combined and operated as one, greatly expediting the work. Whenever it is desired to stamp lozenges with some special letter or design, this is done at the time of cutting them, the plunger being provided with the necessary die.

As the preparation of lozenges has almost entirely passed out of the hands of the retail pharmacist, very few stores are now provided with suitable appliances for making them. When a small number

FIG. 232.

Lozenge apparatus.

FIG. 233.



Base for lozenge apparatus.

of lozenges is wanted extemporaneously, a stiff mass should be made in order to facilitate subsequent drying; it may then be rolled out on a pill-machine or pill-tile, to be cut into the requisite number of

parts, each of which should be given a globular shape and then flattened into a suitable disk, for which purpose the simple apparatus shown in Fig. 232 will be found very convenient. This consists of a brass or steel tube, about 2 or 3 inches long, $\frac{3}{8}$ to $\frac{5}{8}$ of an inch in diameter, and of $\frac{1}{8}$ or $\frac{3}{16}$ of an inch thickness; the bore of the tube must be uniform and smooth and the ends square, otherwise the lozenges will present an irregular appearance. A plunger accurately fitting the tube, preferably made of the same metal, is necessary; it should be of the same length as the tube, and provided with a top about an inch long, exactly covering the outside diameter of the tube. It is desirable that both parts be nickel-plated. To shape the lozenges properly, the globular mass, slightly dusted with starch and sugar or lycopodium, is placed in the cylinder resting upon a metallic base, which consists of a nickel-plated piece of steel or brass, about 2 inches square and $\frac{1}{4}$ inch thick, set in a block of hard wood (see Fig. 233); the plunger having been inserted, it is struck a quick, sharp blow with a mallet, after which the cylinder is raised and the lozenge expelled by slightly tapping the plunger with the mallet. The apparatus shown on page 346, Fig. 234, may also be employed for shaping lozenges, although it is inferior to the above for compressing masses, owing to the projection of the base into the cylinder.

Gelatin lozenges, variously medicated, have been in use for some time, more particularly in Europe. They are composed of a mixture of gelatin, glycerin, and water, holding the medicinal ingredients either in solution or simple admixture. Gelatin lozenges must be made with the aid of heat, and poured, in a melted condition, into suitable moulds; they rapidly congeal. The base is often termed glyco-gelatin, and is made by macerating gelatin with water, on a water-bath, and then adding glycerin; two kinds, containing different proportions of gelatin and glycerin, are in use. A mixture of gelatin, 1 ounce; orange-flower water, $2\frac{1}{2}$ ounces; and glycerin, $2\frac{1}{2}$ ounces (by weight), yields the softer variety, which is very readily soluble in the mouth; whereas a mixture of gelatin, 5 ounces; orange-flower water, 6 ounces; and glycerin, 6 ounces (by weight), evaporated to 15 ounces, produces a much firmer mass, dissolving more slowly, but probably better adapted for stock lozenges in this latitude; in the latter case at least twelve hours' maceration should be given the gelatin and water before adding the glycerin and applying heat.

Gelatin lozenges, while admirably adapted for the exhibition of such substances as cocaine, boric acid, carbolic acid, etc., are totally unsuited for tannin, extract of rhatany, and other agents incompatible with gelatin.

Lozenges intended for immediate use do not require much drying, but those intended for stock must be thoroughly dried before they are put away in glass containers, otherwise they are liable to soften and adhere, and may even become mouldy. The drying is best effected on perforated trays, in a moderately warm room. To avoid

cracking of the edges, which will sometimes occur when lozenges are dried, the addition of a small quantity of glycerin to the water used will be found advantageous, and does not interfere with proper desiccation.

The average weight of lozenges is between 10 and 20 grains, although in the fifteen working formulas of the Pharmacopœia the weight is found to vary between 0.42 and 1.59 Gm. (6½ and 24 grains).

The following is a list of the official lozenges, showing the composition and excipient used:

TABLE OF OFFICIAL LOZENGES.

Name.	Composition of each Lozenge.			Excipient.
Trochisci: Acidi Tannici	Tannic Acid	0.060	Gm.	Stronger Orange Flower Water.
	Sugar	0.650	"	
	Tragacanth	0.020	"	
Ammonii Chloridi	Ammonium Chloride	0.100	Gm.	Syrup of Tolu.
	Extract of Glycyrrhiza	0 250	"	
	Tragacanth	0.020	"	
	Sugar	0.500	"	
Catechu	Catechu	0.060	Gm.	Stronger Orange Flower Water.
	Sugar	0.650	"	
	Tragacanth	0.020	"	
Cretæ	Prepared Chalk	0.250	Gm.	Water.
	Acacia	0.070	"	
	Spirit of Nutmeg	0.030	Cc.	
	Sugar	0.400	Gm	
Cubebæ	Oleoresin of Cubeb	0.040	Gm.	Syrup of Tolu.
	Oil of Sassafras	0.010	Cc.	
	Extract of Glycyrrhiza	0.250	Gm.	
	Acacia	0.120	"	
Ferri	Ferric Hydroxide (dried)	0.300	Gm.	Mucilage of Tragacanth.
	Vanilla	0.010	"	
	Sugar	1.000	"	
Glycyrrhizæ et Opii	Extract of Glycyrrhiza	0.150	Gm.	Water.
	Powdered Opium	0.005	"	
	Acacia	0.120	"	
	Sugar	0.200	"	
	Oil of Anise	0.002	Cc.	
Ipecacuanhæ	Powdered Ipecac	0.020	Gm.	Syrup of Orange.
	Tragacanth	0.020	"	
	Sugar	0.650	"	
Krameriæ	Extract of Krameria	0.060	Gm.	Stronger Orange Flower Water.
	Sugar	0.650	"	
	Tragacanth	0.020	"	
Menthæ Piperitæ	Oil of Peppermint	0.010	Cc.	Mucilage of Tragacanth.
	Sugar	0.800	Gm.	
Morphinæ et Ipecacuanhæ	Morphine Sulphate	0.0016	Gm.	Mucilage of Tragacanth.
	Powdered Ipecac	0.005	"	
	Sugar	0.650	"	
	Oil of Gaultheria	0.002	Cc.	

Name	Composition of each Lozenge.			Excipient.
Potassii Chloratis . .	Potassium Chlorate . .	0.300	Gm.	Water.
	Sugar	1.200	"	
	Tragacanth . . .	0.060	"	
	Spirit of Lemon . .	0.010	Cc.	
Santonin . . .	Santonin	0.030	Gm.	Stronger Orange Flower Water.
	Sugar	1.100	"	
	Tragacanth . . .	0.030	"	
Sodii Bicarbonatis .	Sodium Bicarbonate .	0.200	Gm.	Mucilage of Tragacanth.
	Sugar	0.600	"	
	Nutmeg	0.010	"	
Zingiberis . .	Tincture of Ginger . .	0.200	Cc.	Syrup of Ginger.
	Tragacanth . . .	0.040	Gm.	
	Sugar	1.300	"	

CHAPTER XXX.

COMPRESSED TABLETS AND TABLET TRITURATES.

Compressed Tablets.

THIS class of remedies, closely allied to lozenges, was introduced about fifty years ago in England, and afterward in this country, under the name "compressed pills." The name, however, is erroneously applied, as pills are understood to be made from a previously prepared plastic pill-mass. Compressed tablets have of late years grown greatly in favor with physicians, but it is questionable whether this form of administering medicines is as universally desirable as some manufacturers would claim; while, in some cases, tablets appear more convenient than pills and powders, it would seem as though the prompt action of certain remedies must be considerably impaired by firm compression. They are lenticular-shaped disks, containing one or more medicinal ingredients, obtained by compressing the substance, in the form of a granular powder, into suitable shape, by means of hand- or steam-power, in specially constructed apparatus.

The composition of all compressed tablets should be such that they will readily undergo disintegration and solution in the stomach, hence they should be made with as little adhesive excipient as possible; like pills, they are intended to be swallowed without previous mastication. When several medicinal agents are to be simultaneously exhibited in tablet-form it is essential, as in the case of lozenges and pill-masses, that they be reduced to very fine powder, in order to insure a uniform composition of the mixture, which is subsequently brought to a granular condition by moistening with a suitable excipient and pressing the damp mass through a sieve of 16 or 20 meshes to the linear inch; the granules, still damp, must be thoroughly dried before they are compressed, otherwise they will adhere to the sides of the moulds. In a few cases, when the substance to be compressed possesses no inherent adhesive properties, dilute syrup is employed as an excipient, or a slight addition of finely-powdered sugar is made, and occasionally, although rarely, finely-powdered acacia is added in the proportion of 3 or 5 per cent. of the total weight of the powdered substance. As a rule, water, various mixtures of alcohol and water, or possibly a mixture of glycerin and water, or of glucose and water, are employed as excipients.

Many substances do not require any excipient at all, and can either be bought in the required granular condition or be easily reduced by grinding in a mortar or mill; to this class belong potassium chlorate,

the alkali iodides, bromides, and chlorides, quinine bisulphate, etc. Fine powders are never adapted for compression, since the air which they carry with them when fed into the mould is confined in the small interstices between the particles, and cannot escape upward or downward; hence imperfect compression results; moreover, fine powders often have a tendency to cake, when they cannot be properly fed into the moulds.

While some substances can be compressed quite readily, others present some difficulty, and, in fact, each substance or combination of substances requires special study and treatment. No rule can be laid down as to the use of excipients, and experience alone will prove the operator's best teacher. Charcoal and substances of a similar non-cohesive or spongy character require the addition of about 5 per cent. of powdered acacia, and must be well moistened with a mixture of glucose and water before they can be properly granulated; for such substances it is also preferable to use a No. 12 sieve for granulation. Some authorities recommend the addition of 25 per cent. of sugar in place of acacia; but, although this combination would yield a more soluble tablet, it has been found unsatisfactory in practice. Substances very sparingly soluble in water, such as phenacetin, acetanilid, salol, sulphonal, etc., are improved by the addition of a little starch, and alcohol will serve well to form the mass for granulations.

If tablets, upon solution, are designed to yield effervescent draughts, they may be made by first preparing the corresponding granular effervescent salts (see page 366) and compressing these, or the ingredients upon which the effervescence depends may be granulated separately (preferably in granules of the same size) and then mixed thoroughly just before compression. Thus, if effervescent tablets of lithium citrate or carbonate are wanted, the lithium salt could be granulated with the sodium bicarbonate and a little sugar, while the tartaric acid and the remainder of the sugar should be mixed and separately granulated with alcohol; when both granules are perfectly dry they may be mixed and compressed. All effervescent tablets must be carefully protected against moisture, in air-tight bottles.

Whenever tinctures or fluid extracts are to be administered in compressed tablet form they are preferably evaporated with moderate heat, on a water-bath, to a syrupy consistence, before they are mixed with the other ingredients; if no diluent powder has been prescribed, the syrupy liquid must be incorporated with a mixture of finely-powdered starch and sugar, for the purpose of granulation. Solid extracts may be used either in the form of very fine powder or softened with a little alcohol, diluted alcohol, or water, as the case may be, then incorporated with the vehicle and granulated in the same manner as the syrupy liquids above mentioned.

The preparation of compressed tablets in small quantities may be conveniently accomplished at the dispensing-counter, and various combinations readily furnished on extemporaneous prescriptions. The finely-powdered ingredients, having been intimately mixed and

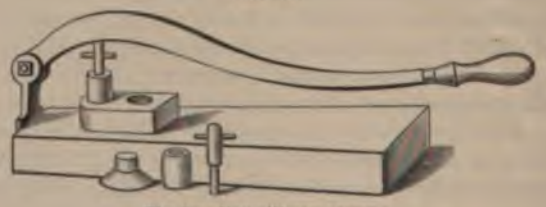
properly dampened, may be quickly passed through a No. 20 or No. 30 sieve, and the granules rapidly dried by rotating them on a sheet of smooth paper placed in a sieve or on a perforated tray over a stove or other heated surface; as soon as dry the granules should be weighed and divided into the requisite number of parts, which will then be ready for compression.

Fig. 234.

Simple mould for compressed tablets.

Different styles of compressors have been designed at various times to suit the purposes of dispensing pharmacists. (See Figs. 234, 235, and 236.) They are all fed on the same principle, and the mode of operating them differs but slightly. The cylinder, base, and piston are usually made of hardened steel, nickel-plated; the base, which is made to project somewhat into the cylinder, as shown in Fig. 234, having been adjusted, the granular substance is carefully fed into the cylinder from a piece of stiff paper, the piston is inserted over the granules, and compression effected either by a sharp blow from a wooden mallet, or by means of a lever, as shown in Figs. 235 and 236. When the tablet has been compressed it can be removed by lifting the cylinder from the base, the tablet adhering to the concave surface of the piston, and gently tapping the piston with the mallet or lever, which expels the tablet. The Smedley compressor (Fig. 235) is provided with a small receptacle, over which the cylinder and piston can be placed and the tablets discharged directly into it.

Fig. 235.



The Smedley pill-compressor.

The greater the pressure applied, the firmer will be the compression, but, at the same time, the slower will be the disintegration of some compressed tablets; hence only sufficient pressure should be used to cause the particles to cohere properly without crumbling when handled or breaking if allowed to fall.

Some substances show a disposition to stick in the mould, and are then removed with difficulty. This tendency can be overcome by the addition of a small quantity of purified talcum and a few drops of liquid petrolatum, which latter may be applied by spraying a solution of it in ether on the granules. By thus lubricating the surfaces of the mould the tablet is readily discharged. In a few cases plain water has been found very serviceable, provided no solvent effect is produced on the substance to be compressed, as, for instance, with phenacetin, salol, naphthalene, etc. If, at any time, a compressed tablet should become fixed in the cylinder or in the concave depression of the piston, or possibly, if fine powder having been inadvertently used, some of it should have been forced between the piston and the sides of the cylinder, and thus fastened have the piston, warm water alone should be used to relieve the trouble; but never should a sharp instrument be employed to loosen the adhering material, as this would be likely to produce rough surfaces or edges, thereby rendering the compressor unfit for use.

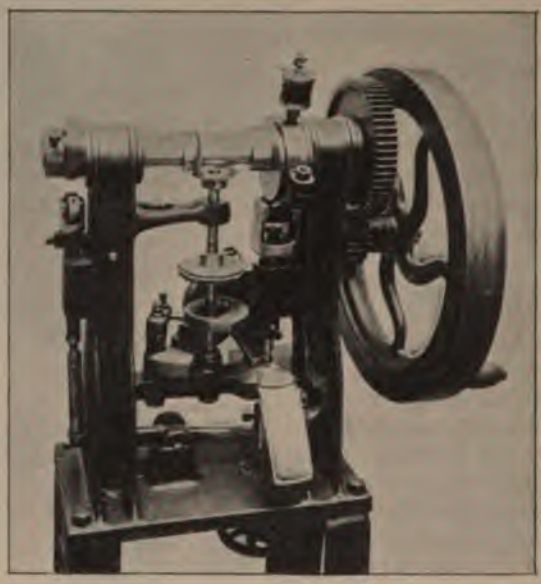
Fig. 236.

Whitall's compressed tablet machine.

For manufacturing compressed tablets on a large scale, special machinery has been constructed to be operated by hand- or steam-power. These machines can be so adjusted that a definite quantity of material will be automatically fed into the mould; therefore, as the pressure applied is uniform, the resulting tablets must be of even weight and thickness. Of the various machines made, the Oriole Tablet Compressor (Figs. 237 and 238) possesses some advantages which adapt it also for smaller operations, such as the manufacture of 50 or 100 one- or two-grain tablets, without the loss of material. The improvement consists in a peculiarly-constructed feeder, the shape of which tends to keep the material constantly at the outlet, hence every particle of it will be discharged into the mould; to prevent any change in the character of the mixture to be compressed, an ingenious stirrer within the feeder keeps the material in constant motion toward the outlet.

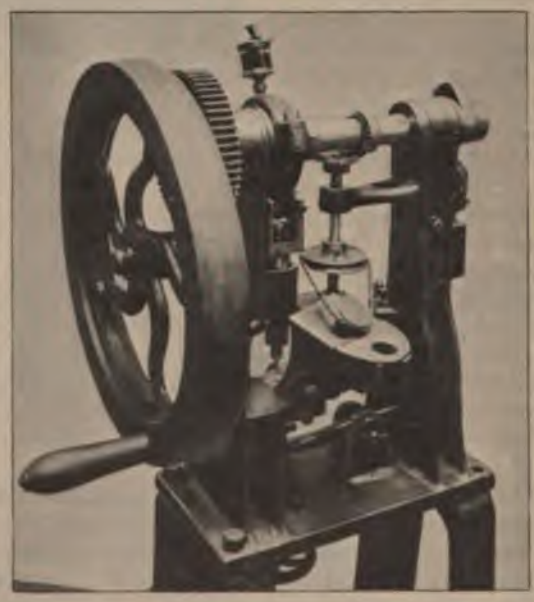
In the "Oriole," as in all automatic tablet machines, the adjustment of the supply of material must be made tentatively; the die or chamber, in which the granules are compressed, is situated below the plate, its capacity being adjusted by means of a screw which controls the depth to which the lower punch shall be allowed to drop in

FIG. 237.



Oriole tablet compressor (front view).

FIG. 238.



Oriole tablet compressor (rear view).

the die. Having adjusted the die approximately, the granulated material is allowed to be fed into it by the hopper and compressed by means of the upper punch situated above the plate and operated by the large wheel on the side; the resulting tablet is then weighed, and, if necessary, the capacity of the die is increased or diminished, as the weight of the first tablet may indicate. The pressure to be exerted upon the tablet is regulated by means of a long screw running perpendicularly through the upper plunger and bearing upon the upper punch. The proper adjustment having been made, the feeder can supply only as much material as the die will hold, hence the automatic supply must be uniform and exact. All automatic tablet machines are so constructed that each tablet as fast as compressed is pushed from the mould into a receptacle suitably provided; in the "Oriole" machine this is done by the hopper as it advances to feed the die.

The dies and punches of all compressors can be had of different sizes, from $\frac{5}{32}$ to $\frac{1}{2}$ inch or more in diameter, to accommodate tablets of various weights ranging from $\frac{1}{2}$ to 30 or 40 grains; they should be perfectly true and highly polished, and must be kept scrupulously clean and dry. If not nickel-plated, they should be coated with a little petrolatum, when not in use, to prevent rusting.

Tablet Triturates.

This class of preparations was introduced, in 1878, by Dr. R. M. Fuller, of New York, no doubt, with a view of administering small quantities of potent remedies in convenient, palatable, and readily-soluble form. Since then some manufacturing firms have made strong efforts to induce physicians to resort to this method of medication for the purposes of office dispensing. That the growth of homœopathic patronage has largely aided the introduction and use of tablet triturates cannot be denied.

Tablet triturates are made by triturating the active ingredient with either plain sugar of milk or a mixture of sugar of milk and ordinary or cane-sugar (usually in the proportion of 4 or 5 parts of the former to 1 part of the latter), and then forming the mixed powders into a paste with alcohol, alcohol and water, alcohol and syrup, or water alone, which paste is pressed into tablets in appropriate moulds. The composition of the liquid excipient to be employed will vary greatly according to the diluent used, the nature of the medicinal ingredients operated upon, and also the quantity to be present in each tablet, the aim being to produce a partial softness in the mixture which will enable the particles to adhere together in the form of a firm, pasty mass. When simply milk-sugar is used as a diluent, water alone will answer as the excipient in most cases, but when a mixture of milk-sugar and cane-sugar is used, a strongly alcoholic liquid excipient is necessary, on account of the ready solubility of cane-sugar in water, the proportion of alcohol being increased as the quantity of cane-sugar is augmented. For most operations at the

dispensing counter, where no special facilities for rapid drying are at hand, a mixture of 5 parts of milk-sugar and 1 part of cane-sugar, together with an excipient composed of 15 volumes of alcohol and 1 volume of water, will perhaps prove most desirable, as the greater volatility of the alcohol insures more rapid drying of the tablets.

It is essential that the sugar be in very fine powder, in order to yield a smooth paste and perfect tablets; and, if the mixture be passed through a No. 120 sieve, before making the paste, the results will be all the better. A few cases will occur in which sugar and other organic matter is inadmissible as a diluent, owing to chemical changes likely to occur; as, for instance, potassium permanganate, silver nitrate, etc.; finely powdered kaolin, or pipe-clay, should then be used with water as an excipient.

Tinctures and fluid extracts, unless strongly alcoholic, are made into tablet triturates with more or less difficulty, according to the amount of fluid to be represented in each tablet, and may require evaporation to dryness with a portion of the sugar, so as to be subsequently reduced to fine powder, prior to converting into a suitable paste. The presence of glycerin, especially if in large proportion, is objectionable, since it keeps the extractive matter soft and prevents proper drying of the tablets. In some instances it will suffice to concentrate the fluid by evaporation and use it, in place of excipient, for moistening the mixed powders; but this plan can only be followed when the proportion of fluid ordered is small or when it has been made with a strongly alcoholic menstruum. Solid extracts can be introduced only in small proportions, and may then be incorporated as indicated under compressed tablets; more than one-fourth or one-third of the total weight of the tablet triturate is not advisable. In such cases, and also in the case of tablets to contain various amounts of tinctures or fluid extracts made with hydro-alcoholic menstrua, a mixture of milk-sugar and starch in varying proportions will be found the best diluent. Substances of a volatile or deliquescent character, or such as are readily oxidized upon exposure to air, are wholly unfit for tablet triturates; hence camphor, creosote, calcium sulphide, arsenic iodide and bromide, potassium citrate, scale salts of iron, phosphorus and the like should never be dispensed in this form.

Automatic machines for making tablet triturates have not yet been constructed, and the apparatus generally used, whether for small quantities at the dispensing counter or in the manufacture of tens of thousands in the laboratory, consists of two plates, as shown in Fig. 239. The plates, although sometimes constructed of metal, are preferably made of hard rubber, the upper one being perforated and the lower provided with a corresponding number of pegs, which fit accurately into the perforations of the upper plate. In order to insure the exact position of the pegs when the upper plate is brought down over them, two guide-pins are fastened to the lower plate, one near each side; these extend above the pegs and enter two corresponding holes in the upper plate. As a rule, the plate moulds are

made to prepare 50 or 100 tablet triturates at one time, although some are provided with 200 or more perforations, and a few with only 25; the perforations vary from one-eighth to three-eighths of an inch in diameter. Since the plates can also be had of different thicknesses, the weight of the tablets made may range from one-half to five grains or more, according to the density of the mass.

FIG. 239.

Hard-rubber mould for tablet triturates.

When a suitable paste has been made the perforated plate is placed upon a level surface, preferably a thick glass plate, and, by means of a horn or rubber spatula, the mass is forced into the holes so as to fill these completely, any excess of material being removed with the spatula; the plate is then reversed and, if necessary, more of the mass is forced into the holes until they are completely filled and both sides present a smooth, solid surface. After the required number of holes have been filled, the upper plate is carefully brought down over the lower one with the marks or numbers at the ends of the two corresponding and, by the aid of the guide-pins, the pegs are pressed into the corresponding holes and the tablets thus forced out, remaining on the ends of the pegs; after a few moments they may be removed, either by inclining and tapping the plate or by carefully brushing them into a suitable receptacle, preferably a bolting-cloth sieve. The tablets should then be dried either by exposure to the ordinary room temperature, protecting them from dust, in closets supplied with circulating warm air, or in small quantities on a perforated tray near a stove or register, as the nature of the medicinal ingredients may permit.

Some manufacturers use an apparatus somewhat differently constructed, as shown in Fig. 240. The two plates are held in frames hinged together and so arranged that the peg-glate can be brought down accurately over the perforated plate carrying the tablets, and

by pressing the pegs down through the perforations the tablets are made to drop out upon a sheet of paper placed underneath for their reception. The exact amount of mass capable of being forced into the holes depends largely upon the pressure exerted by the operator, and varies with nearly every person; besides, different combinations moulded by the same person, being of different specific gravities and compactness, will give different results; the weight of a certain tablet

FIG. 240.

Colton's tablet triturate mould.

having been ascertained, a memorandum should be made of the details regarding combination, diluent, and excipient, for future reference.

Every formula for new tablet triturates must be determined tentatively in order to ascertain the exact amount of sugar of milk or other diluent required. The simplest plan is to weigh off enough of the active ingredients to make a given number of tablets (say 25 or 50); mix this with a quantity of diluent known to be insufficient, moisten with the necessary excipient, and press the mass into the holes of the plate intended to be used. Then moisten more of the same diluent with the excipient, and, with this paste, fill the holes remaining unfilled from the first operation; smooth off both sides of the tablets, place on the ejecting-pegs and force the tablets out. For larger operations the tablets should then be thoroughly dried and weighed, the weight of the dry tablets less the weight of active ingredients used representing the weight of the diluent required to make the given number of tablets. In small operations, particularly those of the dispensing counter, the drying may be omitted, and, instead

an extra number of tablets (4 or 5) made out of the plain diluent, added to the number first obtained, before the whole is thoroughly mixed in a mortar; this extra material is necessary because the first tablets, when worked up again in the mortar, generally form a more compact mass, and hence would prove insufficient for refilling the required number of perforations.

Tablet triturates are, beyond doubt, far more readily disintegrated than compressed tablets, but the latter form has a larger range of applicability, owing to the many variations in quantity and composition; tablet triturates above 5 grains in weight become inconveniently bulky, and, being flat on both sides, are less readily swallowed than even larger compressed tablets of lenticular shape.

Hard-rubber moulds require considerable care in cleaning and in storing them when not in use, in order to preserve the original perfect shape. They should never be exposed to heat, either by using hot water for washing or dry heat for drying them, as the moulds are thereby warped and the accurate adjustment of the pegs and perforations is destroyed; when thus warped, the moulds can only be used with great difficulty, and soon become worthless. A narrow, stiff paint-brush will be found very serviceable in cleaning the moulds, and water at the ordinary temperature should be used for washing the plates; sometimes alcohol, or even acids, may be necessary to remove material tenaciously adhering to the moulds, but never should a sharp instrument be used in the perforations or on the pegs, as the smooth surfaces are likely to be scratched thereby. After the plates have been carefully cleansed and rinsed with cold water they should be dried with a soft towel, the water remaining between the pegs being readily shaken out; when dry, the perforated plate should be placed in proper position on the peg-plate, and the whole laid aside on a level, solid surface, away from heat.

Hypodermic Tablets are simply tablet triturates intended for the convenient preparation of solutions for subcutaneous injection. Since they contain definite quantities of the active agents, they are admirably adapted for physicians' use at the bedside, and are very extensively employed. As a rule, pure sugar of milk or pure cane-sugar is used as the vehicle, although sodium sulphate has also been employed by some manufacturers.

Tablet Saturates differ from tablet triturates only in the manner of introducing the medicinal agents. They are made by first preparing plain sugar of milk tablets, in the moulds already described, and having placed the tablets, when dry, on a glass plate, the desired quantity of tincture, fluid extract, or solution is dropped upon each tablet individually from a pipette. A glass cover is then placed over the tablets and the fluid allowed to saturate them uniformly, after which they are dried in a current of warm air.

CHAPTER XXXI.

POWDERS.

In addition to what has already been said about pulverization, in the chapter on Mechanical Subdivision of Drugs, there remains yet to be considered the administration of medicines in powder form, which, presenting certain advantages, is still largely employed by physicians. The powder form is a most convenient method of giving medicines in the case of very small children and persons who are unable to swallow pills, as well as where the fluid form is unavailable for any reason. It is true, many substances are not suited for administration in powder form, particularly bulky vegetable powders, deliquescent salts, and such as contain large quantities of water of crystallization, as sodium phosphate or sulphate, etc.; but while the fluid form of medicine is probably to be preferred in the majority of cases, the bitter or nauseous taste of some substances becomes more marked in solution than in the dry state. Among the substances best adapted for dispensing in powder form are insoluble chemicals, such as calomel, bismuth salts, sulphurated antimony, some salts of the alkaloids, and vegetable drugs given in small doses, such as ipecac, opium, and catechu. Physicians frequently direct their patients to dissolve or mix the powder in water, and, in such cases, the powder form is preferred on account of convenience or for reasons of economy.

Fig. 241.

Porcelain powder-mortar (sectional view).

Powders, as a rule, are composed of two or more substances; to insure an intimate and uniform mixture they must be triturated in a mortar, preferably made of porcelain, of the shape shown in Fig. 241, this style presenting a sufficiently broad surface at the base, whilst its curved sides prevent the ejection of material during trituration. It is assumed that, in the majority of cases, the individual ingredients are already in the state of very fine powder, and, therefore, only require thorough mixing, which is best accomplished by trituration with light pressure only, so as to avoid caking and sticking to the sides of the mortar; the contents of the vessel should also occasionally be scraped down from the pestle and sides of the mortar, if necessary, as this aids more perfect admixture. Whenever substances which are themselves in

a coarsely powdered or granular condition, are ordered in a powdered mixture, they must be reduced to a very fine powder by themselves, no attempt being made to reduce them in the mixture.

A few general rules will serve for guidance in the preparation of mixed powders. Whenever sugar is one of the ingredients it should be of the kind known as bolted or lozenge sugar. When small quantities of potent or other substances are to be dispensed in powders, they should first be well triturated with a portion of the diluent, and, finally, incorporated with the remainder of the more bulky powders; or, if no diluent has been ordered, they should be triturated with a small quantity of sugar of milk, to insure their more uniform distribution in the mixture. The proper plan is to place about 5 grains of sugar of milk in the mortar, add the active ingredient, and then triturate thoroughly, as, by this means, more accurate subdivision is effected, and none of the active material is likely to adhere to the sides of the mortar. Soft extracts and essential oils must be treated in the same manner.

Whenever physicians prescribe quantities which cannot be weighed conveniently, such as $\frac{1}{6}$, $\frac{1}{10}$, $\frac{1}{24}$, or $\frac{1}{32}$ of a grain, and metric weights less than 10 milligrammes, the plan of preparing a dilution of the substance with sugar of milk, by trituration, in such proportions that a weighable amount of the mixture shall represent the desired quantity of active ingredient, as already indicated on page 309, should invariably be followed, as by this method accuracy of division is best obtained.

Certain substances of a crystalline structure—notably also those of a resinous character—have a tendency to become electrical by friction, particularly if pressure be employed; such bodies are said to be idioelectric, and must be triturated lightly, or, if pressure is necessary to reduce them to fine powder, they must be sprinkled with a little alcohol, whereby the trouble is obviated, or the powder, which adheres firmly to the mortar and pestle, and is apt to fly off in all directions if scraped with a spatula, must be set aside for awhile until the electric condition has disappeared. To this class belong common pine resin, and the resins of guaiacum, jalap, and scammony, also quinine alkaloid, acetanilid, salol, phenacetin, and others. The removal of these in fine powder form from the mortar is attended with more or less difficulty, unless previously slightly dampened.

When substances which differ materially in specific gravity are to be mixed in powder form—as, for instance, bismuth subnitrate with magnesia, sodium bicarbonate with charcoal, or zinc oxide with lycopodium—the best plan is to place the heavy substance in the mortar and incorporate the lighter body gradually by adding small portions at a time. Calcined magnesia and charcoal are also more readily mixed if the charcoal be gradually added to the magnesia with very light trituration; only in this manner can a powder of uniform appearance be obtained. Whenever large quantities of these pow-

ders are to be mixed, perfect blending may be achieved by shaking them together in a bottle for some time, and then passing the mixture repeatedly through a bolting-cloth sieve.

Since some substances when triturated together cause chemical decomposition, attended in a few cases also with explosion, considerable care must be observed in mixing them; the offending ingredient should be reduced to fine powder by itself, and then cautiously mixed on paper with the other powders. Such conditions arise when potassium chlorate or permanganate is to be mixed with organic substances, as sugar, starch, tannin, gum-arabic, and also sulphur and sulphides, or when lead acetate and zinc sulphate or borax and alum are triturated together.

Powders, whether simple or compound, intended for external application, by dusting or insufflation, must be passed through a fine bolting-cloth sieve, and should not then be triturated again before they are dispensed.

In the majority of cases medicines prescribed in powder form are dispensed in divided doses; although absolutely accurate division can only be obtained by weighing, this plan is rarely followed, since practice will soon enable one to omit this tedious method. Usually the operator divides the mixed powder by the eye, either directly on the powder papers or by shaping the powder into a rectangle on a graduated tile, and dividing this into the requisite number of parts; an experienced dispenser is able to make quite accurate divisions from the mortar direct to the paper.

To facilitate the division of doses at the dispensing counter a very neat powder-divider was designed, some years ago, by J. C. Michael, a former pharmacist; it is shown in Fig. 242. The apparatus con-

Fig. 242.

Michael's powder-divider.

sists of a cup with base attached, a set of three dividers, with 8, 10, and 12 wings respectively (one of which is shown in the illustration), and a cap with sliding door. It is operated as follows: The thoroughly mixed powder is placed in the metallic cup, B, and,

after shaking down so as to obtain a level surface, the metallic divider, D, is slipped over the rod, A, and allowed to work its way slowly down to the bottom of the cup; by slight manipulation, such as gently rotating the divider, the powder will be divided into as many equal parts as wings are attached to the divider. The cap, E, which fits snugly over the projecting wings of the dividers, and is held in position by means of a central pin, is next attached, and, the cup having been inverted, the rod, A, is removed by turning the base, C, held by a bayonet-joint, and withdrawing the rod from the centre of the divider. The powder will now be found transferred to the cap, but divided, as before, since the wings of the divider extend beyond the rim of the cup to the full depth of the cap; by bringing the apparatus over the centre of the paper one portion can be deposited at a time by pulling back the slide, F, and allowing the powder to fall upon the paper. It is, of course, important, when placing the cap on the cup, so to adjust it that the edges of the opening be on a line with two of the wings, which is best done with the slide open. By carrying the apparatus from paper to paper and rotating the divider, each succeeding section can be emptied, and thus rapid division of the mixture be effected. The whole apparatus is nickel-plated, which protects it against rust. Very accurate work can be done with this apparatus, and the necessary experience for rapid manipulation is easily acquired.

Another convenient device for those who do not wish to entrust division of powders to the eye is the Diamond Powder-divider. This consists of a nickel-plated, shallow, metal trough, closed at one end and graduated on both sides; the powder having been introduced, a hard-rubber plug is inserted at the open end and pushed up to the graduation indicating the number of divisions to be made. After levelling the surface of the powder by means of an accompanying flat bar, with handle attached and exactly fitting into the trough, the rubber plug is removed and a quantity of the material, equivalent to one dose, as indicated by the divisions of the graduated sides, is transferred to paper by the aid of a spatula of the same width as the interior of the trough. The dimensions of the trough are 9 inches in length, 1 inch in width, and $\frac{3}{8}$ of an inch in depth.

For enclosing the divided doses of powder, either well calendered or parchment paper may be used; the latter is now preferred by many pharmacists, as it offers a protection against the moisture of the air. Even those who use glazed white paper will find either parchment or waxed paper necessary for volatile or hygroscopic substances. Powder papers should be folded uniformly, hence it will be found advantageous to keep in stock a supply of the various sizes already creased. This is readily done by folding the paper over a piece of stiff metal of suitable size, with rounded edges to prevent cutting, in such a manner that a narrow margin, about $\frac{1}{8}$ inch wide, is made on one of the long sides; the straight edge having been brought up against the crease of the margin, both ends are

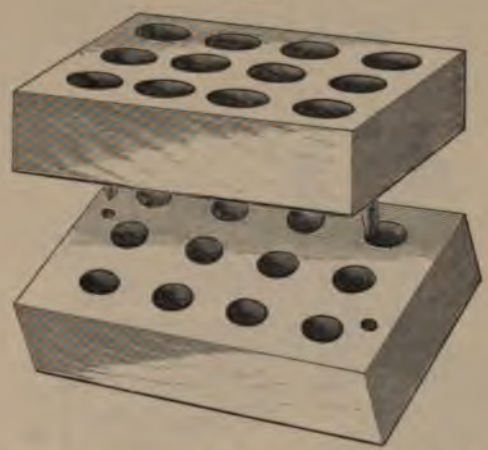
folded back to about the centre of the piece of metal and firmly pressed down with a horn spatula. The two sides are now folded over the edges of the metal plate and also firmly pressed, after which the creases are all opened and the plate is removed. Such creased powder papers not only insure absolute uniformity in size and shape, but have also been found very convenient in economizing time at the prescription counter. Some pharmacists prefer to fold each paper containing the powder over a powder-box or specially constructed adjustable powder-folder. The habit of flattening the powder within the paper by pressing over it with a spatula is a bad one, and should never be followed, as it is apt to cause the powder to cake, and often interferes with its proper administration in liquids. To prevent any of the material from leaving the paper, one of sufficiently large size should be used, that the creases where the sides have been folded over may be pressed down with a spatula; this effectually prevents leakage.

A small number of powders in paper (two or three) are usually dispensed in an envelope, while the regular oblong powder boxes are used for larger numbers. When not divided into doses the powder is dispensed either in round paper boxes (never in paper, unless intended for use at one time) or in wide-mouth bottles; the latter method is necessary if the ingredients are apt to attract moisture or if very volatile substances are present, and will also be found convenient for travelling purposes. When bottles are used, a piece of glazed paper should be inserted between the neck of the bottle and the cork, to prevent particles of the latter from falling into the powder.

While, as a rule, medicines in powder form are administered to the patient either dry on the tongue, or in solution, or mixture with a small quantity of water, physicians frequently direct them to be enclosed in capsules or wafers, with the view of disguising the taste. The filling of definite quantities of a powder into capsules is rather troublesome, on account of the small orifice of the latter, and to facilitate the operation recourse is had to a little device especially designed for that purpose. Small blocks of hard wood are provided with twelve or twenty-four sockets of such depth that the capsules, when placed therein, shall project about one-third above the edge; another piece of wood, with perforations corresponding to the sockets, is placed over the lower block, after the capsules have been inserted, and then, by means of a suitable funnel (of hard rubber or metal), the powder is transferred to the capsules and somewhat compressed with a plunger exactly fitting the throat of the funnel and the capsule. After all the capsules have been filled the upper perforated block is removed and the cover slipped over the projecting ends of each capsule. For the various sizes of capsules different blocks and funnels are required. In Figs. 243 and 244 are shown the blocks and a suitable funnel; the latter has a wide rim flattened on one side and a short tube, whereby the powder is more conveniently fed into

the capsules. The Acme Capsule-filler (Fig. 245) is somewhat different in construction, but is operated in a similar manner.

FIG. 243.



Hard-wood blocks for supporting empty capsules while being filled.

The use of wafers is not so much in vogue in this country as in Europe, but is, in many respects, preferable to capsules; less compression of the material is necessary, and the envelope, made of rice-flour, is more readily disintegrated in the stomach. Sometimes small square or circular sheets of wafer paper are ordered, and the patient is directed to enclose each dose as wanted; this is done by dipping the wafer into cold water, whereby it is rendered flaccid; it is then removed with a spoon, the powder placed in the centre, and, the edges having been folded over, it is swallowed with a draught of water.

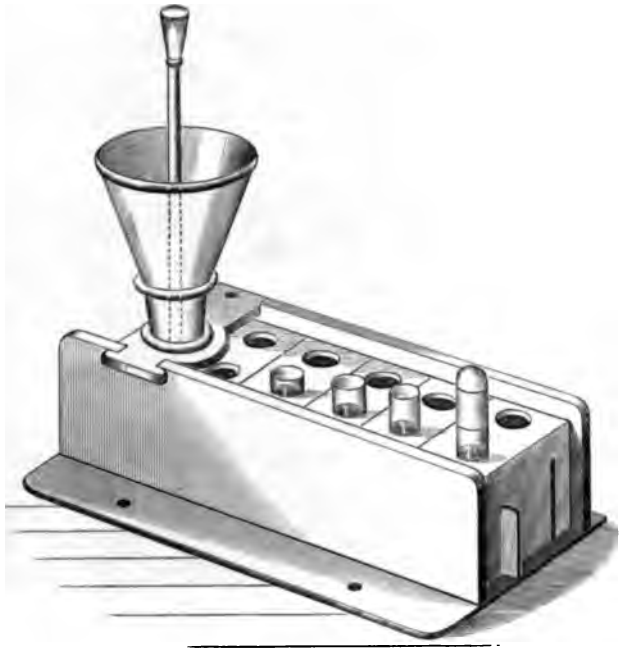
FIG. 244.

Davenport's funnel and plunger for filling capsules.

The small round wafers known as cachets are intended to be filled and sealed by the pharmacists. Various appliances have been proposed, of which that extensively used in Europe in connection with Mohrstadt's cachets is decidedly the most desirable, as it is simple in construction and quickly operated; the device is sold in this country by J. M. Grosvenor & Co., of Boston, as the "Konseal" Filling and Closing Apparatus, and is fully illustrated and described farther on. The use of the word "Konseal" in place of cachets or wafers does not strike one as particularly appropriate, and is to be regretted. The "Konseals," or

cachets, are concave disks made of rice-flour and water; they are of convenient form, perfectly digestible, keep permanently for years, and

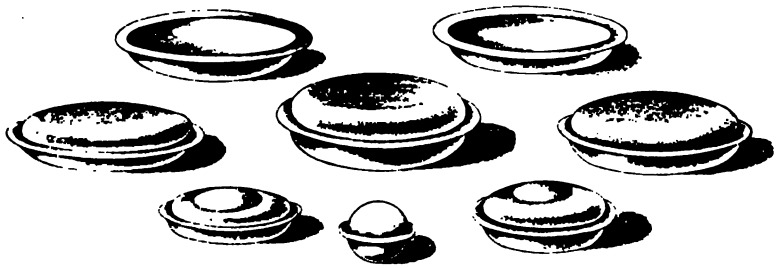
FIG. 245.



Acme capsule-filler.

are prepared in six sizes, as shown in Fig. 246, varying in capacity from 1 to 18 or 20 grains of dry powder.

FIG. 246.

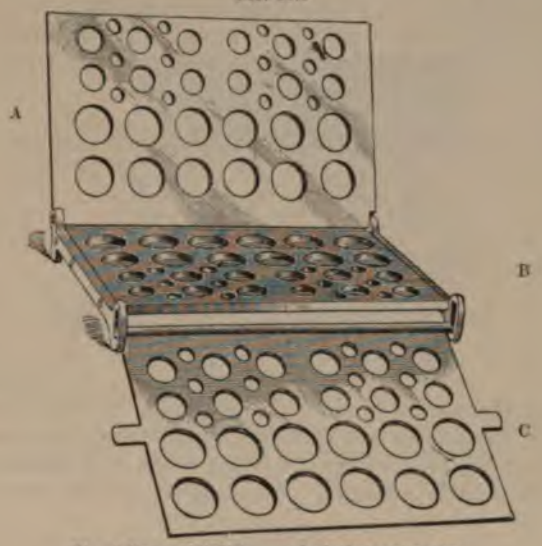


"Konseals" or rice-flour cachets.

The "Konseal" Filling and Closing Apparatus consists of three nickeled plates suitably hinged together (see Fig. 247); the centre plate, B, is provided with 36 concave depressions, to suit the different

sizes of wafers, and the two other plates (A and C) are perforated in a manner to correspond exactly to the depressions in B. The

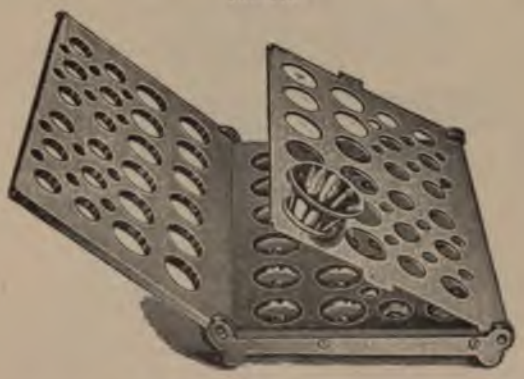
Fig. 247.



The "Konseal" filling and closing apparatus.

wafers are first pressed into the spaces of A and B adapted for the particular size selected; one of the short funnels accompanying the

Fig. 248.



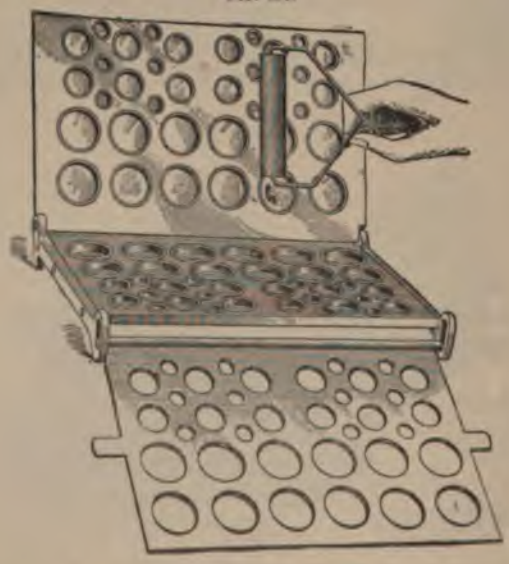
apparatus having been inserted into the proper perforation of plate C, the latter is folded over on to plate B, as shown in Fig. 248. The powders are next poured into the wafers, as shown in Fig. 249, and, if necessary, owing to large bulk, are slightly compressed with the thimble furnished for the purpose; small quantities of the powder

can be conveniently fed into the wafers without the use of funnel or thimble. When the required number of wafers has been filled plate C is turned back from plate B, and the damping roller (not too wet)

FIG. 249.

passed over the wafers in plate A, as shown in Fig. 250, whereby the edges of the wafers are sufficiently moistened to cause them to adhere closely to the other wafers when plate A is closed down over plate B with a little pressure. Finally, on opening the apparatus,

FIG. 250.



the sealed wafers will be found adhering to plate A, and can be easily pushed out by the fingers or with the thimbles.

When powders are to be dispensed either in capsules or wafers it will, of course, be necessary first to make the required number of

divisions on paper, either by weighing or measuring with the eye; in Europe a graduated glass tube with hard-rubber piston is said to be used for the same purpose.

The Pharmacopœia furnishes formulas for the preparation of nine compound powders, but directs the division into doses in only one case. The following is a list of the official powders and their composition:

COMPOUND POWDERS OF THE U. S. PHARMACOPŒIA.

Name.	Composition.	
Pulvis:		
Antimonialis (James' Powder).	Antimony Oxide	33 Gm.
	Precipitated Calcium Phosphate	67 "
Aromaticus	Ceylon Cinnamon	35 Gm.
	Ginger	35 "
	Cardamom (deprived of capsules)	15 "
	Nutmeg	15 "
Cretæ Compositus	Prepared Chalk	30 Gm.
	Acacia	20 "
	Sugar	50 "
Effervescens Compositus (Seidlitz Powder).	Sodium Bicarbonate	2.583+ Gm.
	Potassium and Sodium Tartrate	7.749+ "
	Tartaric Acid	2.250 "
Glycyrrhizæ Compositus	Senna	180 Gm.
	Glycyrrhiza	236 "
	Washed Sulphur	80 "
	Oil of Fennel	4 "
	Sugar	500 "
Ipecacuanhæ et Opii (Dover's Powder).	Ipecac	10 Gm.
	Opium	10 "
	Sugar of milk	80 "
Jalapæ Compositus	Jalap	35 Gm.
	Potassium Bitartrate	65 "
Morphinæ Compositus (Tully's Powder).	Morphine Sulphate	1 Gm.
	Camphor	19 "
	Glycyrrhiza	20 "
	Precipitated Calcium Carbonate	20 "
Rhei Compositus	Rhubarb	25 Gm.
	Magnesia	65 "
	Ginger	10 "

Special Remarks.

In the case of antimonial powder, compound chalk powder, and compound jalap powder, the ingredients being already in a state of fine powder, simple admixture with light trituration is necessary.

Pulvis Aromaticus. Cardamom, deprived of the capsules, are directed, because the latter are inert and cannot be reduced to fine powder; the crushed seed and coarsely powdered nutmeg (best obtained by grating) can readily be brought to a state of fine powder by trituration with about one-half of the cinnamon, using at the same time slight pressure.

Pulvis Effervescens Compositus. The so-called "Seidlitz mixture"

of commerce is not always of the composition prescribed by the Pharmacopœia; hence it is better to make it, as wanted, by mixing 1 part of sodium bicarbonate with 3 parts of Rochelle salt. The alkaline mixture is usually put up in blue papers and the acid powder in white paper. The small wooden measures intended for rapid division of the powders are, as a rule, not uniform; moreover, the quantity of material that can be compressed into these measures varies considerably with the condition of the atmosphere, which renders them unreliable; hence, the prescribed quantities should be weighed for each paper, being 10.333 + Gm. (160 grains) of Seidlitz mixture and 2.25 Gm. (35 grains) of tartaric acid. The powders should be protected against dampness, and it will be found advantageous to dispense the acid in parchment paper.

Pulvis Glycyrrhizæ Compositus. By triturating the oil of fennel with a part of the sugar, before adding the other ingredients, its distribution in the powder is greatly facilitated. The use of oil in place of powdered fennel is advantageous, as the finished mixture can then readily be passed through a No. 80 sieve, and the finer the powder the better it is; moreover, the product will not assume by age that disagreeable odor which has been observed when the powdered seed is used.

Pulvis Ipecacuanhæ et Opii. The Pharmacopœia directs sugar of milk to be used in rather coarse powder, so that the fragments of crystals, being very hard, may serve to grind the vegetable powders to an impalpable condition during the necessarily prolonged trituration. Since the finished product contains 10 per cent. each of ipecac and opium, an average adult dose, 0.648 Gm. (10 grains), of the powder, will represent 0.0648 Gm. (1 grain) of each active ingredient. Dover's powder is a favorite diaphoretic.

Pulvis Morphinæ Compositus. The value of Tully's powder resides in the camphor and morphine present, the liquorice and precipitated chalk serving simply as diluents. In order to secure the camphor in very fine division it must be triturated with a little alcohol and at once mixed with the diluents, the morphine being incorporated by adding to it the other mixed powders in small quantities at a time. The official formula would look better if 20 instead of 19 Gm. of camphor had been directed, on account of the more accurate division of doses. Each gramme of the finished product represents 0.0166 + Gm. of morphine and 0.313 + Gm. of camphor, or 10 grains equal $\frac{1}{6}$ grain of the former and about 3 grains of the latter. Owing to the volatile nature of the camphor the powder should always be dispensed in paraffin or parchment paper.

Pulvis Rhei Compositus. The best plan for thoroughly blending the magnesia with the rhubarb and ginger will be to mix the last-named two powders first, then add the magnesia, in small quantities at a time, triturating without pressure, and, finally, pass the whole mixture through a bolting-cloth sieve.

Triturations.

Under this head the Pharmacopœia recognizes mixtures of remedial agents and sugar of milk, in the form of a very fine powder, made in such proportions that each gramme of the mixture shall contain 0.100 Gm. of the active ingredient, or 1 grain represent $\frac{1}{10}$ of a grain. The general official directions for making triturations are to mix the substance in a mortar, with an equal weight of sugar of milk, both in moderately fine powder, and then to triturate thoroughly together, adding fresh portions of sugar of milk from time to time, until 9 parts of the latter shall have been mixed with 1 part of the substance, and the whole reduced to a very fine powder. The advantage of using moderately fine powder in the beginning consists in the more intimate admixture of the ingredients brought about by the prolonged trituration necessary for reduction to fine powder.

But one trituration is officially designated—namely, "Trituration of Elaterin;" this is a mixture of 10 Gm. of elaterin and 90 Gm. of sugar of milk, made according to the general directions given above.

Oil-sugars.

Powders of this class are chiefly used as correctives or flavoring agents, and are prescribed by physicians under the name Oleosacchara or Elæosacchara. These are extensively employed in Europe, particularly in Germany, but are not recognized in our Pharmacopœia.

The National Formulary gives general directions for preparing them, which are practically identical with those of the official German code. Oil-sugars are composed of powdered cane-sugar and volatile oil only, each drachm of the former requiring the addition of two drops of the latter, the two being thoroughly mixed by trituration; they should be freshly made when wanted. When prescribed, the particular kind is designated by specifying the name of the oil to be used—thus, oleosaccharum or elæosaccharum anisi, menthæ piperitæ, fœniculi, limonis, etc., meaning oil-sugar of anise, peppermint, fennel, lemon, etc.

CHAPTER XXXII.

GRANULAR EFFERVESCENT SALTS.

THE administration of remedial agents in the form of effervescent draughts has become quite popular during the past ten or fifteen years, and, as the solutions are only agreeable when freshly made, it is necessary to have the remedies in convenient form for extemporaneous preparation of the draught. Such a form is presented by the granular effervescent salts of the market. While the Pharmacopœia recognizes but four preparations of this class, a very large number is offered by manufacturers, and, as they are easily made, without elaborate apparatus and appliances, their preparation is within the reach of all pharmacists. The combination consists of the active medicinal ingredients, the effervescent agents, and frequently sugar, to improve the taste. As a base for producing the effervescent draught, sodium bicarbonate, with citric or tartaric acid, or a mixture of the two acids, is employed. Effervescent granules made with citric acid are preferable to those made with tartaric acid, and will keep better, since they are much firmer; as a rule, a mixture of the two acids is used. All ingredients must be dry and mixed in the form of fine powders. The method of granulating the mixture will vary with different operators; while for small quantities, such as the pharmacist is likely to handle, dampening of the powder with 95 per cent. alcohol and then rubbing the paste through a sieve offers the most convenient plan, large manufacturers subject the mixed powders to a temperature sufficiently high to fuse some of the constituents and thus obtain the necessary adhesiveness.

If it is preferred to make granular effervescent salts by heat, as recommended in the British Pharmacopœia, the well-mixed powders should be placed in a pan or dish, which has previously been heated to the desired temperature, and the heat then be continued until semi-fusion has just begun, when the pasty mass must be quickly transferred to the proper sieve for granulation, after which the granules are at once transferred to the drying closet. Unless the pan be properly heated before the powder is placed therein, the material is likely to dry out before it undergoes semi-fusion.

Whenever sugar is present in the mixture to be granulated, care must be observed in the application of heat, to avoid a yellowish coloration of the granules; moreover, the sodium bicarbonate is likely to loose carbon dioxide if heated beyond 72° C. (161.6° F.), thus rendering the preparation deficient in effervescent properties. If alcohol be used to make a pasty mass of the well-mixed powders,

these difficulties are avoided, since a temperature not above 65° C. (149° F.) will be found quite sufficient for drying the damp granules; the stronger the alcohol used, and the stiffer the paste made, the better will be the granular condition of the salt, especially if the subsequent drying can be conducted in drying-closets kept at a constant temperature.

All the required ingredients for effervescent granules must be used in fine powder and thoroughly mixed before an attempt at granulation is made; trituration in a mortar is not desirable, since the resulting pressure is likely to cause reaction between the sodium bicarbonate and acid, hence intimate admixture is best effected by passing the mingled powders repeatedly through a sieve (preferably No. 50). It will also be found advantageous to mix the sodium bicarbonate thoroughly with the sugar (if the latter is to be used) before adding the acid. Strong alcohol only should be used (not below 94 or 95 per cent. by volume) for making a paste that can be just rubbed through the sieve, otherwise the presence of much water will cause loss of carbon dioxide and yield a soft mass, which will not remain in separate granules while drying. The quantity of alcohol necessary will vary with the composition of the mixture; whenever citric acid or salts containing water of crystallization are present a lesser quantity should be used. Some substances contain an unusual amount of water of crystallization; as, for instance, sodium sulphate 55.87 per cent., sodium phosphate 60.31 per cent., magnesium sulphate 51.13 per cent., etc.; this would interfere with proper granulation of the powder, and such salts must, therefore, be rendered either totally, or at least partially, anhydrous, by heating sufficiently before mixing with the other ingredients.

Well-tinned sieves must be used, through which the pasty mass is rubbed with the hands, otherwise the granules will not be perfectly white. A No. 6 or No. 8 sieve yields the most desirable size of granules, from which the fine particles, which are invariably formed along with the coarser, can be readily separated by shaking in a No. 20 or No. 30 sieve.

All effervescent powders must be preserved in well-stoppered bottles, in a dry place, as they are inclined to attract moisture from the air, and thus rapidly deteriorate.

Of the four effervescent salts recognized in the Pharmacopœia, three are directed to be prepared in granular form, and one is simply a dry mixture of the powdered ingredients. The following is a list of the official preparations of this class and their composition:

EFFERVESCENT SALTS OF THE U. S. PHARMACOPŒIA.

Name.	Composition.	
Caffeina Citrata Effervescens	Caffeine	10 Gm.
	Citric Acid	10 "
	Sodium Bicarbonate	330 "
	Tartaric Acid	300 "
	Sugar	350 "

Name.	Composition.	
Lithii Citras Effervescens	Lithium Carbonate	70 Gm.
	Sodium Bicarbonate	280 "
	Citric Acid	370 "
	Sugar, sufficient quantity to make	1000 "
Magnesii Citras Effervescens	Magnesium Carbonate	10 Gm.
	Citric Acid	46 "
	Sodium Bicarbonate	34 "
	Sugar	8 "
Potassii Citras Effervescens	Potassium Bicarbonate	90 Gm.
	Citric Acid	63 "
	Sugar	47 "

Special Remarks.

Caffeina Citrata Effervescens. The Pharmacopœia very appropriately calls this preparation "Effervescent Citrated Caffeine," since no definite chemical compound is formed between the caffeine and citric acid, although the solubility of the former is greatly increased by the presence of the acid.

Lithii Citras Effervescens. This preparation is not officially directed to be in granular form, the well-dried ingredients being simply mixed in fine powder. Lithium citrate is not present in the mixture, but is formed at the time of solution of the powder, nor can the exact quantity of sugar necessary be stated in the formula, since the Pharmacopœia directs the citric acid to be triturated with some of the sugar and the mixture to be thoroughly dried; and, as citric acid contains about 8 per cent. of water of crystallization, the loss of this (wholly or in part) by drying must be replaced subsequently by addition of sugar. A slight excess of citric acid (about $\frac{3}{4}$ per cent.) is present in the finished product, which adds to the agreeably acidulous taste of the preparation when dissolved in water.

Magnesii Citras Effervescens. In order to obtain a granular salt, which is readily and completely soluble, it is important that the official directions be closely followed. The addition of an excess of citric acid to the magnesium carbonate insures the formation of a very soluble acid magnesium citrate, provided the prescribed quantity of water only be used and the temperature of 30° C. (86° F.) be not exceeded during evaporation, otherwise the far less soluble normal salt is apt to be produced, causing trouble in the finished product. The remainder of the citric acid should be powdered separately and then mixed, without pressure, with the sodium bicarbonate and sugar; lastly the finely powdered magnesium citrate is added. The citric acid necessary for complete decomposition of the alkali bicarbonate is derived in part from the acid magnesium salt; although this changes the character of the latter compound, its ready solubility is nevertheless preserved by the newly formed sodium citrate.

In England effervescent magnesium sulphate is extensively used, and a similar preparation is also sold in this country. The British Pharmacopœia directs that 10 parts of crystallized magnesium sulphate shall be heated at 54.4° C. (130° F.) until reduced to about

three-fourths of its weight, when to the powdered residue are to be added 2.1 parts of sugar, 2.5 parts of citric acid, 3.8 parts of tartaric acid, and 7.2 parts of sodium bicarbonate, all in fine powder; the mixture is to be heated at between 93.3° and 104.4° C. (200° and 220° F.) until the particles begin to aggregate, and then assiduously stirred until granules are formed.

Potassii Citras Effervescens. The proportions of citric acid and potassium bicarbonate directed in the official formula are just sufficient for complete decomposition, hence a neutral or normal salt will be formed. When the ingredients are triturated together in a warm mortar, reaction at once sets in, owing to the water present in the acid, hence the drying must be rapidly effected to prevent too great a loss of carbon dioxide. The paste may be formed into granules by rubbing through a No. 6 tinned sieve, or, if dried as a mass, it must be subsequently reduced to a coarse powder in a mortar.

CHAPTER XXXIII.

OINTMENTS AND CERATES.

BOTH classes of these preparations are intended solely for external application; they are of similar composition, of unctuous character, differing however from each other in degree of firmness and fusibility. While the U. S. Pharmacopœia officially recognizes the difference between ointments and cerates, this distinction is not maintained, as a rule, in Europe. The British and German Pharmacopœias designate both classes as ointments; in France the term *pommade* is applied to all ointments made with a purely fatty base, even if a small proportion of wax be present, while the term *onguent* is only used if a resinous or similar substance has been added, the name *cérat* being reserved for mixtures of fat and wax containing at least as much wax as our own cerates.

In the preparation of ointments and cerates it is of importance that perfectly smooth, homogeneous mixtures be obtained, and that the fatty vehicle be absolutely free from rancidity, since they are often applied to tender excoriated surfaces, and would otherwise prove a source of irritation instead of a soothing application. Lumps or gritty particles in ointments indicate unpardonable carelessness on the part of the dispenser.

Ointments and cerates made with yellow wax or resin are less liable to deterioration than when made with white wax, since the latter during the bleaching process undergoes incipient rancidity; they should be preserved in well-glazed, covered porcelain jars and kept in a dry, moderately cool place. The true porcelain jars, although somewhat expensive, are to be preferred, as they are strictly impermeable to grease and can be thoroughly cleaned with hot water and lye whenever empty; the author had a set of these jars in constant use for over fifteen years without ever having an ointment turn rancid in them. Glass stock jars are offered at a much lower price, but will often crack while being cleaned, particularly with hot water, yet they are vastly superior to the ordinary white china or queensware covered jar, since the glazing of the latter soon becomes full of fine cracks, through which the fat permeates and, gradually turning rancid, contaminates the contents of the jar; moreover, no amount of washing will remove the rancid grease entirely from the pores of the jars, hence they soon become unfit for use. The sweet condition of ointments and cerates cannot be preserved without proper care and cleanliness; unfortunately these precautions are only too frequently disregarded by pharmacists.

Ointments.

On account of their soft consistence, ointments are better suited for direct application to the skin by unction, when, becoming liquefied by the heat of the body, they are readily absorbed. They may be conveniently divided into those consisting of plain, unctuous bodies and those composed of the desired remedial agent mixed with a suitable vehicle. The usual vehicle is lard, either plain or benzoinated (see page 191), to which, in southern latitudes or during warm weather, a small proportion of wax, 10 or 20 per cent., is often added; besides lard, lanolin, petrolatum, and various mixtures of oil and wax are also employed. The lard to be used must be free from impurities (see page 190) and correspond to the official requirements. Hydrous wool-fat, or lanolin (see page 191), is, for many ointments, the most desirable vehicle that can be chosen, on account of its ready absorbability and its capacity for taking up large quantities of fluids (aqueous solutions of salts, as well as glycerin and alcoholic liquids); moreover, it is far more stable than lard. Lanolin can readily be combined with its own weight of water, whereas lard takes up only about one-fifth of its weight and soft paraffins not more than 10 per cent. Although petrolatum, vaseline, and similar soft paraffins are well adapted as ointment bases, on account of their indifferent chemical nature, they are ill-suited in some cases, owing to their very slow and imperfect absorption.

The official glycerite of starch is sometimes used by physicians under the name of *plasma* or *plasma glycerini* as a vehicle for ointments, in place of lard or petrolatum. It possesses the advantage of not being of a fatty nature, and hence easily removed by washing with water, and never becoming rancid; but as it is somewhat hygroscopic it must be preserved in well-closed jars. It is especially preferred by oculists for the application of lead acetate, mercuric oxide, and similar substances to the eyelids. A similar but somewhat firmer preparation is the glycerin ointment of the German Pharmacopœia, also known in Europe as glycerolate. It is prepared by rubbing 10 Gm. of wheat starch into a smooth mixture with 15 Gm. of water, adding 100 Gm. of glycerin, and finally a mixture of 2 Gm. of powdered tragacanth and 5 Gm. of alcohol; the whole is heated on a steam bath or over a direct fire with constant stirring until the alcohol has all been dissipated and a transparent jelly-like mass results.

Dermatologists have long been looking for an ointment base or vehicle which, while non-irritating, should not be of a greasy nature if possible, so as to render its use more convenient and agreeable to patients. Numerous substances have been suggested, such as solvine or polysolve and oleite, which are alkali sulpho-ricinoleates, and as such miscible with water, gelatole, a mixture of oleite and gelatin, and similar semi-solid preparations, to be applied in the form of a thin layer or varnish-like coating. The most successful in this respect appears to have been a vehicle composed of casein, glycerin, and soft

paraffin, which is used in Europe under the name *unguentum caseini*. Unfortunately the exact proportions of the ingredients and the mode of combining them are kept a secret by the manufacturers, but, according to their published statements, pure casein is dissolved in water by means of a small quantity of potassium or sodium hydroxide, the solution being then mixed with glycerin and vaseline or soft petrolatum and the resulting white emulsion further preserved by benzoinating it; the finished preparation resembles very soft cold cream or thick condensed milk, and is said to be readily removed from the skin with water.

As regards the mode of preparation of ointments, three distinct methods are followed, namely, by fusion, by incorporation of the medicinal agent with a suitable vehicle, and by chemical action. When ointments are to be made by fusion those constituents having the highest fusing-point, as resin, wax, and spermaceti, should be heated first, and, when nearly melted, the lard or oil added, bearing in mind that, as long as some of the particles remain unmelted, there is no danger from the continued application of heat, which should, however, be withdrawn in time to avoid a rise in temperature of the melted fats (see page 85). Fusion of ointments is preferably performed on a water-bath, in round-bottom pans or evaporating dishes, and, if dirt be present, the melted mixture may be decanted, or, if necessary, strained through cheese-cloth into a previously warmed dish or mortar; the liquid should then be stirred until a homogeneous soft mass results, after which it may be set aside and allowed to stiffen by further gradual cooling. The stirring of melted fats while cooling is essential to insure a perfectly smooth product, since fats are composed of solid and liquid bodies, which, during the cooling process, become partially separated, producing a granular solid on congealing, if allowed to cool at perfect rest, as may be seen in the case of plain lard; moreover, in a mixture of melted fats, those having a higher fusing-point would naturally congeal earlier than the rest; therefore, unless an intimate mixture be kept up by constant stirring separation would ensue and a lumpy ointment result. The point of danger may be said to have been passed when the melted ointment has so far cooled down under continued stirring that a uniform thick, creamy mass is obtained; for stirring a broad wooden spatula will be found advantageous. When large quantities of aqueous liquids are to be incorporated with melted fats, as in the case of rose-water ointment, the liquid should be warmed and then slowly added, with constant trituration, to the mixed fats previously somewhat cooled; otherwise the less fusible constituents will be chilled by the cold liquid and separate in granular form, thus preventing a smooth ointment. The following ointments are officially directed to be made by fusion:

Name.	Composition.	
Unguentum	Lard	80 Gm.
	Yellow Wax	20 "
Aquæ Rosæ	Spermaceti	125 Gm.
	White Wax	120 "
	Expressed Oil of Almond	600 Cc
	Stronger Rose Water	190 "
	Sodium Borate	5 Gm.
Diachylon	Lead Plaster	500 Gm.
	Olive Oil	490 "
	Oil of Lavender	10 "
Picis Liquidæ	Tar	500 Gm.
	Lard	375 "
	Yellow Wax	125 "

The addition of borax to the official rose-water ointment gives the latter a whiter and more creamy appearance, but at the same time interferes with the admixture of certain chemicals, such as calomel, yellow mercuric oxide, etc., causing discoloration of the ointment. Vegetable or mineral powders cannot be mixed in quantity with rose-water ointment without forcing the water out of combination.

Unless the lead plaster for diachylon ointment be fresh it is best to remove the darkened dry exterior, thus obtaining a lighter-colored and softer ointment; the oil must be added when the plaster is nearly melted on a water-bath, and a better mixture will result if the heat be continued for 5 or 10 minutes afterward, so as to blend the oil and plaster more thoroughly. The melted mixture must be stirred until creamy, when the oil of lavender may be added, the whole transferred to a jar and allowed to cool. Diachylon ointment is preferably prepared fresh when wanted, as it does not keep well.

In preparing tar ointment the tar should be free from granular matter and not incorporated with the mixture of lard and wax until the latter has been cooled down to the condition of a smooth, soft ointment. If the tar be added to the hot liquid fats, a granular ointment will result.

Ointments prepared by incorporation of medicinal agents with an appropriate vehicle comprise by far the larger number of official ointments, and practically all those prescribed extemporaneously. Benzoinated lard and simple ointment are alone directed by the Pharmacopœia as vehicles, although physicians frequently use petrolatum or the commercial products known as vaseline and cosmoline; when absorption of the ointment is desired wool-fat, known as lanolin, is decidedly to be preferred. All substances to be mechanically incorporated in an ointment must be in the form either of solution or an impalpable powder; the latter condition, in the case of vegetable substances, can be attained only by passing the powder through a fine bolting-cloth sieve (about No. 120 or 150). The incorporation may be effected either in a mortar or on a heavy glass slab by means of a broad spatula, the finely powdered substance being first mixed with a small quantity of the vehicle, and, when a smooth mixture has been obtained, the remainder added; while an ointment slab is,

as a rule, preferred in this country the mortar is used almost exclusively in Europe, and, for some ointments, is in fact indispensable, particularly when solutions are to be added.

When the quantity of powder to be added is large it will prove advantageous to melt some of the vehicle and mix this with the powder, in a warm mortar, before adding the remainder. Some substances can be conveniently brought into a smooth condition by triturating with a little olive or expressed almond oil, such as calomel, lead carbonate, bismuth subnitrate, zinc oxide, etc., as well as certain crystallizable bodies, like mercuric chloride and silver nitrate; for the latter a little oil is decidedly better than water, since, upon the gradual evaporation of the latter, a return to the crystalline state is probable, giving rise to the presence of minute gritty particles which would cause irritation. Opium should be rubbed smooth with about an equal weight of water, and then at once incorporated with the fatty vehicle before the paste begins to dry; solid extracts are treated in like manner, enough water or, in some cases, diluted alcohol being used to produce a thick, syrupy liquid. Some salts may be dissolved in water, provided they are very soluble, as potassium iodide, while others must be reduced to an impalpable condition by trituration, as lead acetate, tartar emetic, zinc sulphate, etc. Red mercuric oxide, iodoform, naphtalene, and boric acid may be triturated with a few drops of alcohol, in a mortar, until rendered impalpable; camphor should be powdered, by the aid of alcohol, just before it is to be used, and added to the ointment after all other ingredients have been incorporated, since it is soluble in the fat and materially softens its consistence, which, in the case of solid extracts, would interfere considerably with their perfect admixture.

Iodine, before admixture of fats, is preferably dissolved in a small quantity of water, with the aid of a little potassium iodide, as it cannot readily be rubbed into a very fine powder by itself; the addition of alcohol is sometimes employed to facilitate the division of the iodine, but this plan never yields so satisfactory an ointment.

When iodine is ordered in combination with mercurial ointment, the addition of potassium iodide is unnecessary, as chemical union will take place between the iodine and mercury; the proper plan would be to rub the iodine into a fine powder and then add a portion of the mercurial ointment, triturating well until the iodine has disappeared and the change in color indicates that union has taken place, after which the remainder of the ointment may be incorporated. If an extract, such as belladonna or stramonium, is also to be added, this should be separately mixed with some of the fat and then added to the previous mixture, whereby a much better ointment will be obtained.

Substances which are wholly or partly soluble in fats, such as menthol, salol, chrysarobin, benzoic and carbolic acids, aristol, naphtol, and the like, should be triturated, in fine powder form, with a portion of the vehicle liquefied by heat, and, after addition of the remainder, the mixture must be continually stirred until cold. If

chloral, thymol, naphtol, or salol be ordered, together with camphor, in an ointment, the two substances must be triturated together until an oily fluid results, which can then be readily incorporated with the vehicle.

Alkaloidal salts may be incorporated in ointments in solution in water or, if present in large quantity, may be added in form of a very fine powder; but whenever pure alkaloids are ordered by physicians these should be triturated with a small quantity of warm oleic acid, before they are mixed with the fatty vehicle, as more intimate distribution is thus effected than if the alkaloids be merely rubbed into a smooth paste with olive or almond oil.

Glycerin should never be used in place of oil or water to produce a smooth paste with vegetable or mineral powders, because, although derived from fats, it can be incorporated with them permanently only with difficulty. When glycerin in considerable quantity is ordered to be added to an ointment consisting chiefly of lard or a mixture of lard or oil with wax, the addition of a small proportion of anhydrous wool-fat, in place of a like quantity of the regular vehicle, will overcome all difficulty of incorporation. A similar expedient will prove most valuable when large quantities of aqueous fluids are to be incorporated in ointments, or in the case of alcoholic liquids which, ordinarily, mix with fats with great difficulty. The pharmacist, in preparing ointments containing fluids, must so combine the constituents that a permanent homogeneous mixture results, from which the fluids will not separate on standing.

It will be found very convenient to keep on hand anhydrous wool-fat for the purposes above stated; it is readily prepared by heating some of the commercial lanolin (containing about 30 per cent. of water) on a water-bath, until it ceases to lose weight.

When two or more ointments having different fusing-points are to be mixed, the firmer should always be rubbed down by itself first, and the softer fats be then incorporated in small quantities at a time, otherwise an imperfect mixture results. A mixture of mercurial ointment with lard or simple ointment offers an example; in cold weather this mode of procedure is all the more imperative; it should also be followed when anhydrous wool-fat is to be mixed with softer fats, as the former is usually somewhat tough.

Whenever substances likely to attack metal are ordered in ointments the incorporation with the fatty vehicle should never be made with steel spatulas, but always with horn or rubber-coated ones; the latter can now be had quite pliable, and are admirably adapted for ointments containing tannic acid, iodine, mercuric chloride, etc.

The Pharmacopœia directs the following eighteen ointments to be prepared by incorporation of the medicinal agent with the fatty vehicle; of the latter, except in one case, benzoinated lard and the official simple ointment alone are used:

Name.	Active Ingredient.		Vehicle.
Unguentum:			
Acidi Carbolici,	Carbolic Acid	5 per ct.	Ointment.
Tannici,	Tannic Acid	20 "	Benzoinated Lard.
Belladonnæ,	Extract of Belladonna Leaves	10 "	" "
Chrysarobini,	Chrysarobin	5 "	" "
Gallæ,	Powdered Nutgall . . .	20 "	" "
Hydrargyri,	Mercury	50 "	Lard and Suet.
Ammoniati,	Ammoniated Mercury . .	10 "	Benzoinated Lard.
Oxidi Flavi,	Yellow Mercuric Oxide . .	10 "	Ointment.
Oxidi Rubri,	Red Mercuric Oxide . .	10 "	"
Iodi,	Iodine	4 "	Benzoinated Lard.
Iodoformi,	Iodoform	10 "	" "
Plumbi Carbonatis,	Lead Carbonate . . .	10 "	" "
Iodidi,	Lead Iodide	10 "	" "
Potassii Iodidi,	Potassium Iodide . . .	12 "	" "
Stramonii,	Extract of Stramonium Seed .	10 "	" "
Sulphuris,	Washed Sulphur . . .	30 "	" "
Veratrini,	Veratrine	4 "	" "
Zinci Oxidi,	Zinc Oxide	20 "	" "

The official directions accompanying each formula and the general directions given above are sufficiently explicit to insure satisfactory ointments, therefore further comment is unnecessary, except in two or three cases.

The extinguishment of mercury by means of oleate of mercury, in the preparation of mercurial ointment, is readily effected by trituration in a mortar on a small scale, but large manufacturers probably follow the plan of prolonged agitation in suitable vessels. When the globules of mercury have become invisible the mixture of lard and suet, melted and partly cooled, is easily incorporated. The commercial variety of mercurial ointment, known as one-third mercury, is nearly 17 per cent. weaker than the official, and should not be used in prescriptions. In very warm weather mercurial ointment may become almost liquid, and is then liable to loose mercury by separation, hence the necessity for keeping it in a cool place. When mercurial ointment is prescribed in divided doses by physicians, each portion should be separately weighed on paraffin or parchment paper, and then folded as directed in the chapter on powders.

Ointment of red oxide of mercury is apt to become discolored when rancid: hence, if it is to be kept on hand for some time, a better vehicle than lard and wax may be employed. A mixture of one part of yellow wax and three parts of castor oil will not turn rancid, and, if with this be incorporated the proper proportion of finely powdered red mercuric oxide, the ointment can be kept for months without change.

The addition of sodium thiosulphate (hyposulphite) to ointment of potassium iodide is for the purpose of preserving its white appearance; without this addition it will turn yellow and finally brownish, owing to a gradual liberation of iodine. In the formula of the British Pharmacopœia potassium carbonate is directed to be added for the same purpose.

Of the ointments made by chemical action, the official ointment of

mercuric nitrate is a striking example. When lard oil is heated and mixed with nitric acid, the former undergoes oxidation at the expense of the acid, olein being converted into a new compound, solid at ordinary temperatures, known as elaidin, the term olein being usually applied to the fluid constituent of fat and fixed oils. The incorporation of the solution of mercuric nitrate subsequently with the elaidin is simply a mechanical admixture, the solution having no chemical effect whatever on the fat. It is essential that the nitric acid be of official strength, and that heat be reapplied, if necessary, to complete the oxidation of the fat; the heat of a boiling-water-bath only should be used, however, as over a direct fire decomposition of the fat is apt to ensue and a dark brown compound result, whereas, on the water-bath, not more than a deep orange color is produced. The oxidation of the lard oil goes on quietly, and is known to be ended when effervescence ceases and a soft solid mass is obtained upon cooling. The solution of mercury in nitric acid can be made in the cold, and may be warmed finally to expel any colored gas that has been retained. If the fat has been properly oxidized and cooled down, as directed in the Pharmacopœia, the mercuric nitrate solution will not suffer reduction when added, and a bright lemon-yellow ointment will result, if the mixture be stirred until cold with a glass or wood spatula. Ointment of nitrate of mercury should never be brought into contact with metal, to avoid precipitation of finely divided mercury.

Another instance of chemical reaction in the preparation of ointments is in the original formula for Hebra's ointment; lead oxide is heated with olive oil, in the presence of water, until all the oxide has chemically combined with the fatty acids derived from decomposition of the oil, the newly-formed lead oleate remaining intimately mixed with the excess of oil and the glycerin liberated from the fat. The decomposition taking place will be more fully explained under the head of Saponification in Part III. The original Hebra's ointment differs from the official diachylon ointment in containing some free glycerin.

Ointments should always be dispensed in glass or porcelain jars provided with suitable covers; if the latter be of metal or wood, a disk of heavy paraffin paper should be inserted to avoid contact with the fatty substance. Under no circumstances, *except when intended for immediate use only*, should ointments be put up in wood-boxes, as the fat will readily penetrate the material, and thus become exposed to oxidation by the air. When ointment jars are returned to be refilled they should be carefully wiped out with soft paper and washed thoroughly before the new ointment is put in; a fresh disk of paraffin paper should also be inserted and a new label be put on the jar if the old one has become soiled.

To cleanse the apparatus in or on which ointments have been prepared the best plan is first to wipe off all remaining grease with clean sawdust or soft paper and then to wash it well with warm water and lye or soap. In the case of iodoform ointment a few drops of oil of

turpentine will remove the characteristic odor readily, as already stated on page 316.

Cerates.

This class of preparations differs from ointments in the presence of a considerable proportion of wax, and frequently also of resin or oleoresinous substances. Cerates are intended to be applied as dressings, usually spread on linen or soft leather; while they become somewhat softer at the temperature of the body, they do not liquefy, and are intended to act only locally. What has been said before regarding the preparation of ointments by fusion, and also their preservation, applies likewise to cerates; owing to their firm consistence the latter are not well adapted to admixture with powdered substances, although fluids are sometimes incorporated with them.

The Pharmacopœia recognizes six cerates, which, with the exception of the cerates of lead subacetate and of spermaceti, are usually carried in stock by the pharmacist. Two of the official cerates contain resin, and, in these, yellow wax is also used; hence there is no danger of rancidity. The other four are made with white wax and lard or oil; if benzoinated lard were used in place of plain lard, these cerates would keep much better.

The following is a list of the official cerates, showing their composition:

Name.	Composition.	
Ceratum	White Wax	30 parts.
	Lard	70 "
Camphoræ	Camphor Liniment	10 "
	White Wax	30 "
	Lard	60 "
Cantharidis	Powdered Cantharides	32 "
	Yellow Wax	18 "
	Resin	18 "
	Lard	22 "
	Oil of Turpentine	10 "
Cetacei	Spermaceti	10 "
	White Wax	35 "
	Olive Oil	55 "
Plumbi Subacetatis	Solution of Lead Subacetate	20 "
	Camphor Cerate	80 "
Resinæ	Resin	35 "
	Yellow Wax	15 "
	Lard	50 "

Camphor cerate contains but 2 per cent. of camphor, and is used only in the preparation of Goulard's cerate; the amount of camphor is not sufficient to impart marked medicinal properties to the cerate.

In the formula for cantharides cerate the powdered cantharides are directed to be macerated with oil of turpentine for forty-eight hours before adding the lard, wax, and resin, previously melted together, for the purpose of facilitating the subsequent solution of the blistering

principle in the fats, as turpentine is known to exercise a ready solvent effect on cantharidin, the active principle of Spanish flies. The excess of turpentine is dissipated during the subsequent digestion on the water-bath, and, as the powdered cantharides are not removed by straining, it is important that the mixture be continually stirred, when removed from the bath, until cool. In Great Britain, France and Germany this cerate is known as Emplastrum Cantharidis or E. Vesicans.

The incorporation of solution of lead subacetate with camphor cerate, in the preparation of Goulard's cerate, is more easily accomplished, especially in cold weather, if the camphor cerate be first softened a little by trituration. The finished product contains about 5 per cent. of basic lead acetate and 1.6 per cent. of camphor.

The official resin cerate congeals as a perfectly homogeneous mixture upon cooling without stirring on account of the large proportion of resin and wax present; stirring of the melted and strained mixture is, in fact, not desirable in this case, as it incorporates considerable air. Resin cerate gradually grows tougher by age.

CHAPTER XXXIV.

LINIMENTS AND OLEATES.

THESE preparations are closely allied to those described in the preceding chapter, being also intended only for external use.

Liniments.

Liniments are fluid or semi-fluid preparations, usually in the form of solutions, although, in some instances, merely mechanical mixtures, the solvent or vehicle being either a fixed or volatile oil or alcohol, which latter is sometimes mixed with water. They are always applied to the skin by friction, and, when mechanical mixtures only, require to be well agitated before they are applied. The present Pharmacopœia recognizes nine liniments, of which four are of a fatty nature, while five are alcoholic or hydro-alcoholic solutions; with two exceptions, they are usually prepared extemporaneously, although they keep well.

When fixed oils are shaken with aqueous solutions of alkalies, partial decomposition of the fat takes place, and an emulsion-like mixture results, in which the remaining oil is kept in perfect suspension by the newly formed soap; such liniments thicken considerably by age, which it is intended to provide against in the official formula for ammonia liniment, by the addition of alcohol. If the fixed oils used are fresh and perfectly sweet, they are but little acted on by alkalies in the cold, hence the preparation of a perfect liniment becomes difficult.

The following is a list of the official liniments:

Name.	Composition.	
Linimentum Ammoniæ	Ammonia Water	35 Cc.
	Cotton-seed Oil	60 "
	Alcohol	5 "
Belladonnæ	Camphor	5 Gm.
	Fluid Extract of Belladonna, sufficient to make	100 Cc.
Calcis	Lime-water } of each	50 Cc.
	Linseed Oil } of each	50 Cc.
Camphoræ	Camphor	20 Gm.
	Cotton-seed Oil	80 "
Chloroformi	Chloroform	30 Cc.
	Soap Liniment	70 "

Name.	Composition.	
Linimentum Saponis	Powdered Soap	7 Gm.
	Camphor	4.5 "
	Oil of Rosemary	1 Cc.
	Alcohol	75 "
	Water sufficient to make	100 "
Saponis Mollis	Soft Soap	65 Gm.
	Oil of Lavender	2 Cc.
	Alcohol	30 "
	Water sufficient to make	100 "
Sinapis Compositum	Volatile Oil of Mustard	3 Cc.
	Fluid Extract of Mezereum	20 "
	Camphor	6 Gm
	Castor Oil	15 Cc.
	Alcohol sufficient to make	100 "
Terebinthinæ	Resin Cerate	65 Gm.
	Oil of Turpentine	35 "

Special Remarks.

The cotton-seed oil of the market does not seem well adapted for the preparation of ammonia liniment, separation into two distinct layers invariably occurring in the official mixture; if the cotton-seed oil be replaced in part—15 or 20 per cent.—by olive oil, and particularly common olive oil, which usually contains some free fatty acids, a much more satisfactory liniment will be obtained. Ammonia liniment is also known as volatile liniment, from the volatile nature of the alkali used. Camphorated ammonia liniment, recognized in the German and French Pharmacopœias, is made from camphor liniment in place of plain fixed oil.

In the preparation of camphor liniment, the solution of the camphor can be materially hastened by placing it, with the oil, in a strong bottle and, after corking the same securely, digesting the mixture on a water-bath at a moderate heat.

Chloroform liniment of the United States Pharmacopœia differs materially from that of the British Pharmacopœia; the latter is a mixture of equal volumes of chloroform and camphor liniment. A very popular preparation, known as Compound Chloroform Liniment, is composed of one volume each of chloroform and tincture of aconite and six volumes of soap liniment.

Powdered soap, as directed in the Pharmacopœia, is to be much preferred in making soap liniment, on account of the variable quantity of moisture present in the official soap. The liniment can be more quickly prepared if the soap be heated with about three times its weight of water, in a dish, on a water-bath, until a uniform gelatinous mass results, which will dissolve almost immediately when mixed with one-half the prescribed quantity of alcohol; the camphor and the oil of rosemary having been dissolved in the remainder of the alcohol by agitation, are then added to the soap solution, followed by sufficient water to make the required volume. The official directions to set the liniment aside in a cool place for twenty-four hours, and then to filter, are for the purpose of getting rid of the

sodium palmitate always present in castile soap, which is but sparingly soluble in the menstruum, particularly in the cold.

The official turpentine liniment is also known as "Kentish" liniment; only a moderate heat should be employed to melt the resin cerate, so as to avoid volatilization of the oil of turpentine, which must also be added in small quantities, with constant stirring, until a smooth, uniform, opaque mixture results.

Oleates.

This class of preparations has been in use by physicians in this country since 1872. Normal oleates are true chemical compounds of oleic acid with metallic oxides or alkaloids, but the oleates medicinally employed are simply mixtures of such normal oleates with oleic acid or some other diluent. The proportion of any particular metallic oxide or alkaloid to be dissolved in oleic acid may vary with the views of the physician; but, in the case of normal oleates, a certain proportion cannot be exceeded. The expressions 2, 5, 10, or 20 per cent. oleate are used to indicate that 2, 5, 10, or 20 parts of the respective alkaloid or metallic oxide are present in every 100 parts of the finished product. The following table shows the amount of base combined with oleic acid in 100 parts of the respective normal oleates:

Normal	Oleate of	Iron (ferr'c)	8.9	per cent.	of	anhydrous ferric oxide.
"	"	Copper	12.7	"	"	cupric oxide.
"	"	Zinc	12.9	"	"	zinc "
"	"	Bismuth	22.2	"	"	bismuth "
"	"	Mercury	28 4	"	"	mercuric "
"	"	Lead	29.0	"	"	lead "
"	"	Morphine	50.3	"	"	morphine
"	"	Atropine	50.6	"	"	atropine.
"	"	Cocaine	51.8	"	"	cocaine.
"	"	Quinine	53.46	"	"	quinine.
"	"	Strychnine	54.22	"	"	strychnine
"	"	Veratrine	61.15	"	"	veratrine
"	"	Aconitine	69.6	"	"	aconitine

(The last named two proportions are based on the formulæ given by Prescott for pure aconitine and veratrine.)

From these normal oleates weaker preparations can readily be made by admixture with the desired diluent, according to the well-known rule already given on page 66. Multiply the desired quantity by the desired percentage strength and divide the product by the percentage of the normal oleate; the quotient will indicate the quantity of normal oleate to be used, and subtracting this from the desired quantity gives the weight of the diluent necessary.

Solutions of alkaloidal oleates are best prepared by triturating the prescribed quantity of dry alkaloid in a small dish, with the necessary weight of oleic acid, and heating the mixture somewhat on a water-bath until perfect solution results; they are, as a rule, of 2 per cent. strength, with the exception of morphine and cocaine,

usually of 5 per cent. strength, and quinine frequently prescribed of 25 per cent. strength. As alkaloidal oleates are always intended to act constitutionally, and therefore must be absorbed, oleic acid only should be used in their preparation, and no other diluent be added. The necessary amount of alkaloid and acid for any given weight of solution, can be quickly calculated by the rules given on page 114 under Percentage Solutions.

The solution of metallic oxides in oleic acid is effected very slowly even with the aid of heat, hence they are preferably prepared by mutual decomposition, by adding an aqueous solution of the metallic salt to a solution of an alkali oleate. The precipitated metallic oleates are then washed with water to free them from the newly formed alkali salt; with the exception of mercuric oleate, they may all be washed with hot water, two or three washings being quite sufficient, but for mercuric oleate only warm water must be employed to avoid decomposition. Metallic oleates are usually prepared of normal strength, as they keep better in this form and can be subsequently diluted as wanted. With the exception of mercuric oleate, the metallic oleates are intended for local medication, hence benzoinated lard or soft paraffins are employed as diluents. As mercuric oleate is intended to be absorbed, no other diluent than oleic acid should be used; sometimes, however, physicians prefer dilution with lanolin.

A solution of castile soap is very often used as the alkali oleate in the preparation of metallic oleates, especially those of lead, copper, and zinc; but since the soap is a sodium oleopalmitate, instead of pure sodium oleate, the resulting metallic oleates will also be contaminated with palmitates; in practice, this slight impurity is generally disregarded, and can be reduced to a minimum by allowing the soap solution to stand in a cool place for twenty-four hours and then filtering. The strength of the soap solution generally used is one ounce of dry soap to the pint. Purer metallic oleates can be obtained by using a solution of sodium oleate made directly from official oleic acid by the following process: Warm, in a capacious dish, 1217 grains of oleic acid to about 60° or 65° C. (140° to 149° F.) and add slowly 192 grains of official soda (90 per cent.) dissolved in a mixture of two fluidounces of distilled water and six fluidrachms of alcohol, stirring constantly until the acid is neutralized, which is best ascertained by testing a small portion of the resulting soap, dissolved in alcohol, with a few drops of phenolphtalein solution—not more than a faint pink tint should appear. The soap is next dissolved in three pints of water and filtered. A solution of potassium oleate of about the same strength may be obtained if to one pint of boiling water be added 410 grains of potassium bicarbonate and afterward 1156 grains of oleic acid, the mixture being boiled until the acid has all been taken up and a clear soap solution results, which, when cold, is diluted to three pints by addition of water. To one pint of either of these alkali oleate solutions may be added one-

half pint of a metallic salt solution containing the following quantities of the salt:

For one pint of sodium oleate solution:

Lead Acetate, crystallized	273 grains.
Copper Sulphate, crystallized	180 "
Zinc Sulphate, crystallized	207 "
Mercuric Nitrate	237 "

For one pint of potassium oleate solution:

Lead Acetate, crystallized	259 grains.
Copper Sulphate, crystallized	170 "
Zinc Sulphate, crystallized	197 "
Mercuric Nitrate	225 "

The United States Pharmacopœia recognizes but three oleates, all made by direct solution of the active ingredient in oleic acid; they are:

Oleate of mercury containing 20 per cent. of mercuric oxide, oleate of veratrine containing 2 per cent. of veratrine, and oleate of zinc containing 5 per cent. of zinc oxide.

The first named is of the consistence of firm butter, the second is a liquid, and the last named is like a soft ointment.

Powdered oleate of zinc should be the true normal oleate, but the commercial article is frequently mixed with an excess of zinc oxide; it is best prepared by the process suggested by Mr. Beringer, which is as follows: Warm the sodium oleate solution (see page 383) to 43° C. (109.4° F.), and to it add slowly, with constant stirring, the solution of zinc sulphate, collect the precipitate on a moist filter, wash thoroughly with water, and dry, on bibulous paper, at a temperature of not above 38° C. (100° F.). In order that the oleate, when dry, may be obtained in white friable masses which can easily be passed through a sieve as an impalpable unctuous powder, it is important that the temperature during precipitation be maintained between 38° and 43° C. (100° to 110° F.).

Under the names of ointments of the various oleates, manufacturers have for some time offered a class of preparations in regard to which some confusion exists, as the vehicle as well as the proportion of the oleate used varies with different manufacturers; the vehicle is either benzoinated lard or soft or firm petrolatum, hence the consistence may vary considerably. The term "ointment of any oleate, 5, 10, or 20 per cent.," can have but one meaning as far as the active ingredient is concerned, namely, that the finished product contains 5, 10, or 20 parts of the respective normal oleate in every 100 parts of the ointment, and not 5, 10, or 20 parts of the alkaloid or metallic oxide, as is frequently supposed. Ointments of oleates are officially recognized in only one instance, the ointment of zinc oleate of the British Pharmacopœia, which is composed of equal parts of 10 per cent. zinc oleate and soft paraffin.

CHAPTER XXXV.

PLASTERS AND SUPPOSITORIES.

Plasters.

PLASTERS are preparations intended for external application, which, although firmer and more tenacious than cerates, become adhesive by the heat of the body, and can be made to serve the double purpose of offering both support and medication to the parts to which they are applied. They are firm solids at ordinary temperature and cannot be spread without the aid of heat, but retain a certain degree of flexibility when applied to the body. The base or mass of all plasters made by pharmacists is either simple-lead plaster or a mixture of the same with wax, resin, and gum-resins; in large manufactories a rubber mass is specially prepared from caoutchouc and certain aromatic resins, which is greatly to be preferred on account of its flexibility and adhesiveness. It admits of the ready incorporation of various medicinal agents and possesses many advantages over the ordinary lead-plaster and resinous bases. In the preparation of the rubber plaster-base the crude India rubber of commerce is first freed from impurities, by steaming and continuous washing with warm water, in suitable machinery, until all foreign matter has been removed, after which it is repeatedly passed between heavy steel rollers kept at a temperature of about 35° or 37° C. (95° or 98.6° F.); during this kneading process the rubber gradually softens and assumes a plastic condition which fits it admirably for the incorporation of very finely powdered olibanum and resin or Burgundy pitch, this being also effected between warm, smooth rollers.

The preparation of plasters by pharmacists is very similar to that of cerates, being preferably conducted with water-bath heat, those constituents having the highest fusing-point being first introduced into the pan or dish, and others of greater fusibility being gradually incorporated. All wholly or partly volatile substances, as oleo-resins or essential oils, must be added last, and non-fusible substances must be incorporated in the form of very fine powder whenever possible; as gum-resins are frequently added to plaster mixtures, and as they cannot be reduced to fine powder without injury, they must either be treated in coarse powder with alcohol, and the resulting solution of resinous matter then evaporated to a thick, syrupy consistence, as in the case of asafetida, myrrh, and galbanum, or be emulsionized with diluted acetic acid and then evaporated until the liquid hardens on cooling, as in the case of ammoniac. In either case the concentrated

liquid should be added to the fused mixture when it begins to cool, the mass being well stirred to insure uniform distribution.

Fluid and solid extracts must be incorporated as in the case of ointments, the former after evaporation to a syrupy consistence, the latter after softening down with diluted or strong alcohol, as the case may be. As in the case of ointments, the extinguishment of metallic mercury in plasters is most conveniently effected by trituration with mercuric oleate.

If any foreign matter, such as sand, pieces of wood, and the like, should be found in the melted plaster, this is best removed by decantation or straining, which must always be done before the insoluble and non-fusible substances are added; if straining be resorted to, it will be advisable to perform this operation with the smallest bulk possible, the strained material being always received in a warm pan or dish.

If plasters are to be preserved for stock, they are usually rolled into cylindrical pieces of convenient thickness weighing about 4 or 8 oz.; this operation is performed on a slab or board previously moistened with water or expressed oil of almond; these sticks or rolls should be wrapped in wax- or paraffin-paper to protect them from the air.

Although, with two exceptions, the term plaster is officially applied to the mass or combination to be spread upon leather or muslin, it is more extensively used in trade to designate the finished spread plaster, ready for application. The spreading of plasters has almost entirely passed out of the hands of the pharmacists, hence it does not now appear necessary to describe and illustrate the various appliances which, 20 or 25 years ago, were considered a very essential and important part of every educated pharmacist's outfit. Plaster masses, official and otherwise, can now be purchased of reliable quality, spread on muslin or other material, in one- and five-yard rolls, or in definite and convenient sizes, from large manufacturers, and there is to-day no more reason why a pharmacist should be compelled to make and spread his own belladonna plasters than that he should return to the spreading of his own adhesive plaster, as was done years ago. Moreover, plasters are prescribed but rarely now by physicians, and, when some new combination is ordered, the pharmacist will probably have little difficulty in spreading the plaster of fair quality and appearance by following a few general directions here given.

For extemporaneously spread plasters the best material is soft white leather, the kind known in the trade as plaster skin. A piece should be cut one inch larger each way than the size of the plaster ordered; thus a 4 x 6 plaster would require a piece of leather 5 x 7 inches; now prepare four strips, one-half inch in width, of stiff paper, preferably glazed, and having previously prepared the plaster mass on a water-bath, as directed above, apply the paper strips to the rough side of the plaster skin in such a manner that the desired space shall remain uncovered, and carefully pour the melted plaster on the

leather, smoothing the surface with a warm spatula, or by holding the spread plaster near a stove or furnace-register and allowing the soft material to run smooth. Then, having placed the spread plaster on a level surface, with a quick motion remove the paper strips before the plaster surface hardens, so that a clean half-inch margin around the plaster proper may be obtained. In place of a spatula, the little roller shown in Fig. 251 may be used with advantage for smoothing

FIG. 251.

Plaster-roller.

the spread plaster mass; it should be dipped in hot water, so as to become warm, before it is used, and then be moistened with a mixture of one volume of glycerin and two volumes of water to prevent adhesion.

If the paper strips be attached before the melted mass is ready to be applied, the paste is apt to dry out, when subsequent removal of the paper from the rough leather becomes difficult, and hence some pharmacists prefer to moisten the strips with a damp sponge just previous to spreading the plaster mass; this plan has been found very advantageous. Instead of using paper strips, some prefer to cut a frame of thin cardboard, with a central opening of the required shape and size of the plaster, which is tacked down on the plaster skin. The amount of material necessary for spreading a plaster of the required thickness need not exceed 12 or 15 grains for each square inch, or about 0.165 Gm. for each square centimeter. Plaster-spreading requires manipulative skill, and practice alone can bring success; yet the writer has seen some plasters spread by students in his laboratory, who had never before seen the operation, that would have been a credit to any first-class pharmacy.

Mammary or breast plasters are always made circular in form, about 8 inches in diameter, with a 1-inch margin; a hole 1½ inches

in diameter is cut in the centre, and from this point to the outer edge the plaster is slit to admit a folding over the breast. Such plasters are preferably spread on chamois skin, which is softer.

Porous-plasters, which have become very popular, differ from ordinary spread plasters in having numerous small holes punched through them, rendering them more comfortable for prolonged application, by allowing exhalations of the skin to pass off freely. They are prepared on an extensive scale by special machinery.

Fly-plaster is the name frequently applied to cantharides or blistering cerate when the same has been spread upon adhesive plaster ready for use. The spreading of the cerate is done in the manner already outlined for regular plaster masses, except that heat is unnecessary, since the cerate is sufficiently soft to permit of being spread by simple pressure of a spatula; on cold winter days the spatula may be somewhat warmed with advantage. The amount of blistering cerate necessary for a given space should not exceed 10 or 12 grains for each square inch, or about 0.120 Gm. for every square centimeter. As fly-plasters are not intended for prolonged application, ordinary muslin or adhesive plaster will answer on which to spread the cerate, the latter material being preferable on account of the adhesive edges, which serve to keep the plaster from slipping about. A piece of tarletan, a trifle larger than the surface of the cerate, should be firmly pressed over the same, which, while not interfering with the blistering action of the cantharides, protects the skin from being much soiled, and prevents any of the cerate from getting under the skin if the blistered surface should be lacerated by sudden removal of the plaster.

The *Pharmacopœia* still recognizes 11 plaster masses and 2 spread plasters, very few of which, however, are used by physicians at the present day, except court and adhesive plasters for surgical purposes, and possibly belladonna plaster for its anodyne effect. The official directions for preparing the various plasters are explicit, requiring little or no additional remarks; with care and observance of the precautions before stated, good results will be obtained.

Lead plaster is, strictly speaking, a chemical compound—lead oleate or lead soap—the manufacture of which will be more fully explained in connection with the subject of saponification. It enters either directly or indirectly into the composition of all but three of the official plasters.

The proportions of ammoniac and lead plaster present in the official ammoniac plaster with mercury will vary, depending entirely upon the character of the gum-resin, which is frequently found in commerce of very indifferent quality, mixed with dirt and other foreign matter.

The following is a list of the pharmacopœial plasters showing their composition:

Plaster Masses.

Name.	Composition of 100 parts.	
Emplastrum: Ammoniaci cum Hydrargyro	Ammoniac	?72 parts.
	Mercury	18 "
	Oleate of Mercury	0.8 "
	Diluted Acetic Acid	?
	Lead Plaster	?
Arnicæ	Extract of Arnica Root	33 parts.
	Resin Plaster	67 "
Belladonnæ	Extract of Belladonna Leaves	20 parts.
	Resin Plaster	40 "
	Soap Plaster	40 "
Ferri	Ferric Hydrate, dried	9 parts.
	Olive Oil	5 "
	Burgundy Pitch	14 "
	Lead Plaster	72 "
Hydrargyri	Mercury	30 parts.
	Oleate of Mercury	1.2 "
	Lead Plaster	68.8 "
Opii	Extract of Opium	6 parts.
	Burgundy Pitch	18 "
	Lead Plaster	76 "
Picis Burgundicæ	Burgundy Pitch	80 parts.
	Olive Oil	5 "
	Yellow Wax	15 "
Picis Cantharidatum (Warming Plaster.)	Cerate of Cantharides	8 parts.
	Burgundy Pitch	92 "
Plumbi	Lead Oleate	100 parts.
Resinæ (Adhesive Plaster.)	Resin	14 parts.
	Lead Plaster	80 "
	Yellow Wax	6 "
Saponis	Soap, dried	10 parts.
	Lead Plaster	90 "

Spread Plasters.

Capsici.
Ichthyocollæ.

Capsicum and isinglass or court plasters are the only plasters officially directed to be spread, the former on muslin and the latter on taffeta. The body of the capsicum plaster is the official resin plaster, the surface of which is brushed over with oleo-resin of capsicum, 0.25 Gm. being contained in every space 10 centimeters square, or about ¼ grain in every square inch. The material to be used in making court plaster is a mixture of gelatin 5 parts, water 60 parts, alcohol 40 parts, and glycerin 1 part; it is applied to the taffeta after the surface has been painted with sizing. A coating of tincture of benzoin is afterward applied to the back to render the plaster waterproof.

Suppositories.

Suppositories are solid, medicinal preparations designed to be introduced into the rectum, vagina, urethra, or nose; when intended for

the two last-named, they are usually termed bougies. They are of such consistence that, while retaining their shape at ordinary temperatures, they will slowly melt at that of the body or liquefy in the presence of moisture. The usual shape of rectal suppositories is that of a cone with a rounded apex (see Figs. 252 and 253), but the diffi-

FIG. 252.

Rectal suppositories. (For adults.)

FIG. 253.

Rectal suppositories. (For children.)

FIG. 254.

The Wellcome-shape suppository.

culty of readily introducing these into the rectum, on account of the resistance offered by contraction of the sphincter muscle, has led to the suggestion of a new shape by H. S. Wellcome, of London, as shown in Fig. 254, the great advantages of which become apparent when it is remembered that the bulbous end is inserted into the rectum first, and that as soon as the greatest diameter, which is about one-half inch from the point, has been passed, expulsion of the suppository is impossible, by reason of the very contractile force of the sphincter, which renders retention of the ordinary conical shape often so difficult.

FIG. 255.

FIG. 256.

FIG. 257.

Vaginal suppositories.

FIG. 258.

Urethral bougie.

Vaginal suppositories are made either globular or similar to the rectal suppositories, as shown in Figs. 255, 256, and 257, while, for urethral and nasal bougies, the pencil-shape, seen in Figs. 258, 259,

FIG. 259.

The Wellcome-shape urethral bougie.

and 260, has been adopted, the last-named being about one-third as long, but twice as thick as the urethral bougies.

FIG. 260.

Nasal bougies.

Suppositories are intended to insure a slow and uniform diffusion of their medicinal constituents to those internal parts to which they may be applied, and the choice of vehicle is made accordingly. The best substance for the preparation of suppositories is undoubtedly cacao-butter, or oil of theobroma, on account of its low fusing-point and bland, non-irritating properties. A mixture of glycerin and gelatin, known as glycerin-jelly, is also frequently employed, being particularly desirable for vaginal suppositories and nasal and urethral bougies, on account of its ready miscibility with water. It is admirably adapted for the exhibition of solid extracts, as those of opium, belladonna, and ergot, and such substances as chloral hydrate, but cannot be used in connection with tannic acid, owing to the fact that tannic acid combines with gelatin, forming an insoluble compound. The proportions best adapted for general purposes are gelatin 20 parts, glycerin 40 parts, and water 80 parts, the whole to be reduced by evaporation to 100 parts. For some purposes, these proportions may have to be changed; thus, for hygroscopic drugs, such as potassium or sodium iodide and bromide, chloral hydrate, etc., a mixture of gelatin 10 parts, water 40 parts, and glycerin 15 parts, evaporated to 25 parts, will be found much better. Glycerin-jelly is prepared by soaking the gelatin in the water for a few hours, or over night, in a covered dish, then adding the glycerin and evaporating on a water-bath to the required weight.

In Great Britain a mixture of curd soap (soap made with animal fat) and glycerite of starch is frequently employed as a vehicle, made in the proportion of 30 parts of the glycerite to 100 parts of soap, sufficient powdered starch being added to make a stiff paste.

The *Pharmacopœia* recommends the weight of rectal suppositories

to be about 1 gramme (15 grains), of vaginal suppositories about 3 grammes (45 grains), and of urethral bougies about 1 gramme (15 grains), but these sizes are frequently exceeded in practice to 2 or 3 times the above specified weights.

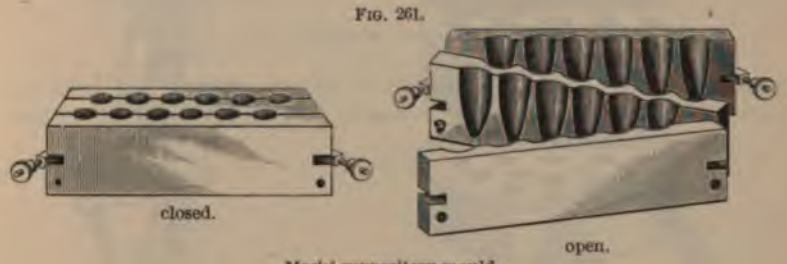
Since suppositories are, like ointments, simply mechanical admixtures of the medicinal constituents and a vehicle, the former must always be incorporated in the form of an impalpably fine powder or in a state of solution, solid extracts being rubbed into a smooth paste with water. On account of the peculiar application of suppositories, it is important that no coarse or gritty particles should ever be contained therein. They are made either entirely by hand, by casting in appropriate moulds, or by cold compression in suitable apparatus.

Hand-made suppositories are, as a rule, not so exact and uniform in shape as those moulded, although some pharmacists have attained considerable perfection and dexterity in following this convenient method. The usual plan is to effect an intimate mixture of the active ingredients and vehicle in a mortar, by forming them into a uniform mass, and transfer the mass to a graduated tile to be divided into the required number of equal parts, which are then properly shaped with the fingers. To prevent adhesion of the mass to the tile or fingers, it may be dusted with some finely powdered starch or a mixture of starch and lycopodium. This method, of course, excludes the use of glycerin-jelly, and, if the mass shows a disposition to crumble, the addition of a few drops of castor oil will overcome the difficulty, rendering the mass plastic. (One of the best vehicles for making suppositories by hand, or by cold compression, is a mixture of cacao-butter 5 parts, castor oil 1 part, and yellow wax 1 part, which fuses at about the same temperature as cacao-butter.)

For casting suppositories in moulds it is necessary to have the mass in a fluid state. If carefully and skilfully followed, this method yields the most perfectly shaped and finished suppositories that can be made; but it requires practice to insure success, presenting more difficulties than any other method. If the fluid mass be poured into the moulds too warm, immediate separation of the insoluble ingredients occurs, which settle in the apex of the cone. If allowed to cool too fast, it will not flow properly, and fill the moulds imperfectly; the proper condition of the mass is reached when the fluid is of a thin, syrupy consistence and a slight film begins to form on the surface. High heat should be avoided in preparing the mass, a low, water-bath heat being amply sufficient for melting the cacao-butter or glycerin-jelly. Any solid extract to be added should be softened down with a little water, mixed with a small quantity of melted vehicle on a tile, and transferred to the dish or capsule containing the remainder of the melted vehicle, which has been removed from the water-bath and allowed to cool somewhat. By stirring with a glass rod or narrow steel spatula the extract will become uniformly incorporated, after which any solid ingredient, in very fine powder, may be added and thoroughly mixed; the fluid mass is then

immediately poured into well-chilled moulds, with constant stirring to prevent separation. It is important that no heat be applied to the mass after the addition of the medicinal constituents lest separation occur, particularly in the case of extracts, which cannot afterward be successfully overcome. The moulds must be perfectly clean and dry, having been previously well chilled by placing them on ice; there will then be no occasion whatever for dusting them with lycopodium or other substance. If the fluid mass is of the right consistence and the mould cold, it will immediately congeal and contract on being poured into the moulds, but sufficient time should be allowed for the suppository to harden throughout, otherwise some trouble may be experienced in removing them; in winter twenty or thirty minutes will suffice, whereas forty minutes or longer may be necessary in summer unless the mould, after having been filled, be placed in an ice-chest. Various styles of moulds are in use among pharmacists, those known as divided moulds, opening either horizontally or vertically, being preferred on account of the convenience with which they can be taken apart and cleaned. Figs. 261, 262, 263, and 264 represent four different styles of moulds, from all of which the suppositories can be quickly removed by bearing slightly with the finger against the conical ends after the moulds have been opened.

Fig. 261.



Maris' suppository mould.

Fig. 262

Wirz's suppository mould (open).

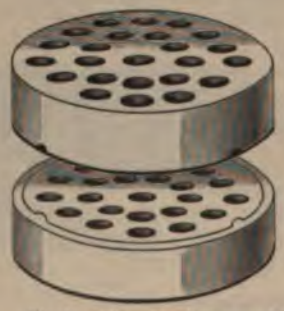
The numerous difficulties attending the casting process have led many pharmacists to abandon this process in favor of cold compression. The chief advantages of the compression method are the saving of time, and the absence of all danger of overheating and of separation of extracts and other ingredients, while the suppositories are uniform in composition and leave nothing to desire in appearance, although the finish is possibly not quite so perfect as in care-

fully-cast suppositories. The mass for compression is prepared in a mortar, as for hand-made suppositories, and, when a uniform mixture has been obtained, it is removed and cut up into small pieces, which are placed in the hopper or barrel of the compressor.

FIG. 263.

See's suppository mould.

FIG. 264.



Blackman's suppository mould.

FIG. 265.

The Archibald suppository machine.

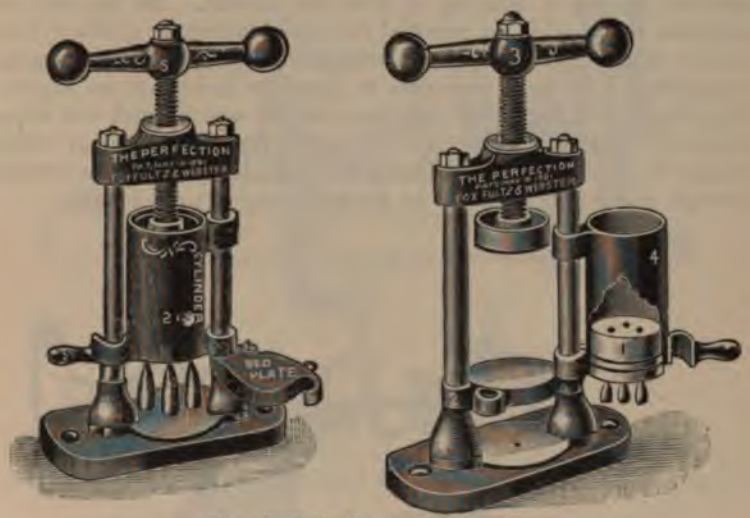
The first successful compression mould for dispensing purposes was that known as the Archibald mould (see Fig. 265), which is still used by many. The only objection to this mould is the tedious removal of the finished suppository; the adhesion of the mass to the sides can be readily overcome, however, by swabbing the mould with a pledget of cotton dampened with glycerin between every two compressions.

The two apparatuses shown in Figs. 266 and 267 are improvements on the Archibald mould in so far that 3 rectal suppositories can be compressed at once, whilst the finished product is easily and quickly removed. They differ from each other only in the position

of the compressor, one being perpendicular and the other horizontal; both, however, require considerable effort to force the mass through

FIG. 266.

a, closed. *b*, open.



The "Perfection" suppository mould.

the small openings in the top of the moulds into the moulds proper underneath, which is the only objection that can be urged against them.

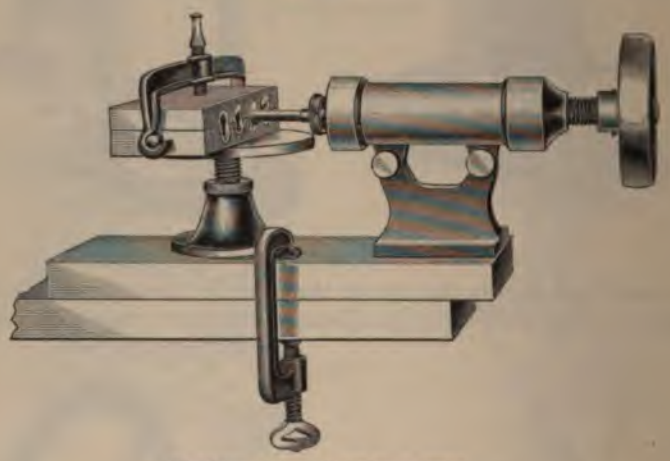
FIG. 267.

Whitall's suppository machine.

Each of the three compression machines is provided with a set of 3 suppository moulds (2 rectal, 30 and 15 grains, and 1 vaginal) and 1

bougie mould. In the Archibald machine the moulds are placed in a swinging bed, which is secured under the cylinder by means of a lever, and after the suppository has been compressed the swinging bed is loosened, the mould taken out and opened, and the suppository removed by gently pushing it with the thumb. In the two other machines the moulds are screwed into the lower part of the cylinder, resting firmly against an iron bed-plate; to remove the compressed suppository it is only necessary to open the bed-plate, as shown in Fig. 266, *a*, and, by one or two turns of the screw, push the suppositories out of the moulds. For the compression of nasal or urethral bougies a plate is put into the cylinder and a small tube attached, through which the mass can be forced to any desired length.

FIG. 268.

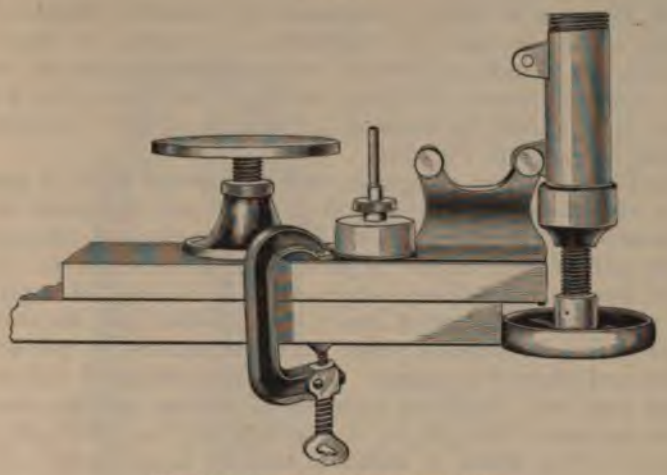


The Genese suppository compressor.

For cold compression of the Wellcome-shape suppositories a machine has recently been perfected which is easily filled and operated, and produces excellent results. The suppositories are compressed in paper shells, which permit of their ready removal from the moulds and avoid all contact with the fingers. The mode of filling the moulds, as seen in Fig. 268, is entirely different from that of other compression machines; the mass, being first carried from the cylinder to the point of the mould, then fills the paper shell perfectly and compactly, as the mould is made to recede under the influence of the pressure from the cylinder. As the moulds come in sets of four or six attached to a plate, the suppositories can be made very rapidly with this machine. In Fig. 269 is shown the cylinder swung back, with the cap removed, for the purpose of filling it with the material to be compressed.

Bougies, made with glycerin-jelly, are cast in special moulds, such

FIG. 269.



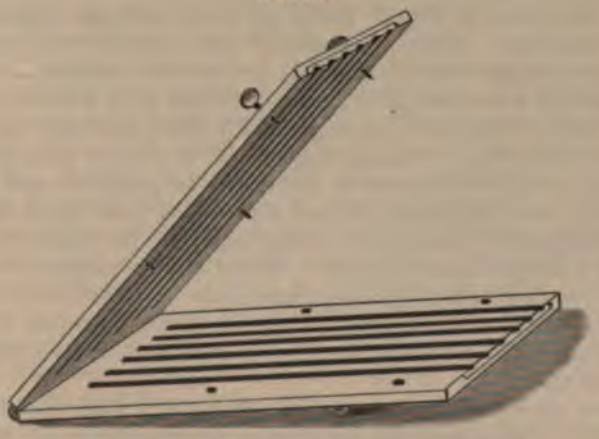
The Genese suppository compressor, open.

as are shown in Figs. 270 and 271; the tubes are usually swabbed with a woollen rag carrying some liquid petrolatum or olive oil, to prevent

FIG. 270.

Mould for gelatin bougies.

FIG. 271.



Mitchell's urethral bougie mould.

adhesion of the material. When made with cacao-butter or soap and starch, they can be either compressed or formed by hand. Nasal bougies should be about 38 millimeters ($1\frac{1}{2}$ inches) in length and 6 millimeters ($\frac{1}{4}$ inch) in diameter, while urethral bougies are usually made 100 millimeters (4 inches) in length and from 3 to 4 millimeters ($\frac{1}{8}$ to $\frac{1}{6}$ inch) in diameter. The ends of both are somewhat pointed, as shown in Fig. 258.

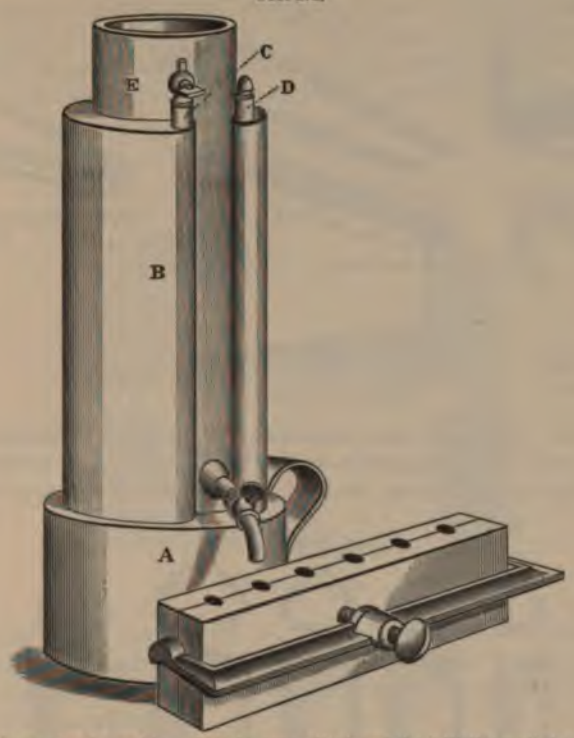
The Pharmacopœia recognizes only one special kind of suppositories, viz., those of glycerin, and gives general directions for the preparation of all others. Glycerin suppositories are composed of 90 per cent. of glycerin and 10 per cent. of sodium stearate. In the official formula, crystallized sodium carbonate is dissolved in glycerin, on a water-bath, after which stearic acid is added and the heat continued until effervescence ceases, when the solution is poured into moulds and allowed to congeal. The three grammes of sodium carbonate used will yield 6.4 grammes of sodium stearate, according to the equation $2HC_{18}H_{35}O_2 + Na_2CO_3 10H_2O = 2NaC_{18}H_{35}O_2 + 11H_2O + CO_2$, which is sufficient to form a solid mass with 60 grammes of glycerin, the water and carbon dioxide being dissipated. Owing to the very hygroscopic nature of glycerin, the suppositories must be either wrapped in tinfoil or dispensed in small straight vials without a lip; some manufacturers coat them by dipping them into melted paraffin, which protects them against the air, but has the disadvantage of possibly failing to be removed by the patient before insertion, in which event the suppository could not act, as the heat of the body is not sufficient to melt paraffin.

A very ingenious apparatus has been devised by Dr. Genese, of Baltimore, for the purpose of casting glycerin suppositories of the "Wellcome" shape in pure tinfoil shells, which can be quickly and hermetically sealed, and thus all contact with the hands and air be avoided. The apparatus and mode of using it are illustrated in Fig. 272. A is a tin or copper boiler of about one-pint capacity, with handle attached. The top is extended into a double-wall cylinder, B, open to a certain width on one side for its entire length, and serving as a steam or hot-water jacket; it is provided with a steam-vent at C and a safety-valve at D, through which the boiler can also be replenished with water, when necessary. E is a heavy glass (or metal) cylinder in which the glycerin mass is to be prepared and kept; it fits snugly into the jacket, B, and is provided near the bottom with a small spigot for feeding the melted mass into the tinfoil shells previously arranged in the moulds. When not in use the cylinder, E, can be covered with a ground-glass plate or closed with a rubber stopper, by which arrangement a supply of the mass can be kept on hand, requiring only slight heating to liquefy it when suppositories are to be cast.

Where glycerin suppositories are frequently sold, this apparatus will prove a most desirable addition to the appliances for rapid and

neat dispensing, and, being always ready for use, will save much labor and annoyance.

FIG. 272.

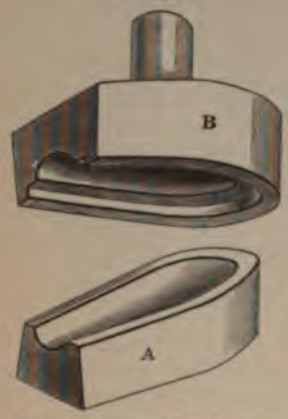


Apparatus for making glycerin suppositories of the "Wellcome" shape.

In Fig. 273 is shown a little device for sealing the edges of the tinfoil shells, which can be made of either metal or rubber. The construction is such that, when the shell containing the solidified glycerin mass has been placed in the lower section, A, and the upper section, B, is brought down over it with a little pressure, the projecting lateral edges of the shell (see Fig. 274) are folded by means of the grooves; by then reversing the shell, a second fold is tightly creased in the same manner, and all air thus excluded. The shells being filled only to within about $\frac{3}{16}$ of an inch of the mouth, the projecting front edges can be lapped over before the lateral edges are folded, and thus the whole shell be hermetically sealed. Fig. 275 represents one of the tinfoil shells filled and sealed; glycerin suppositories thus preserved have been found to keep excellently in ordinary boxes, during hot weather, and upon removal from the shells were found firm and free from moisture.

Suppository shells made of gelatin or butter of cacao have been introduced for the convenience of the dispenser, but are not used to

Fig. 273.



Apparatus for sealing tinfoil suppository shells.

Fig. 274.

Tinfoil shell for glycerin suppositories.

Fig. 275.

Glycerin suppository in tinfoil shell sealed.

any extent. The medicinal ingredient is intended to become mixed with the material of the shells as the latter melts, but, as this is uncertain, they should never be used in case the direct application of

Fig. 276.

Suppository shells, made of cacao-butter.

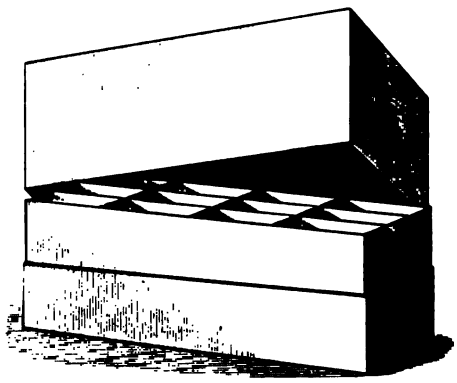
Fig. 277.

Gelatin suppository shells.

the active agent might irritate; for the introduction of boric acid, iodoform, aristol, etc., they are, however, well adapted. In the case of butter of cacao shells (see Fig. 276) they are preferably filled with

a mixture of the active ingredient and grated butter of cacao, and the top sealed either with a warm spatula or a little stiff mucilage of acacia. The gelatin shells, see Fig. 277, may be conveniently sealed by moistening the margin of the lower half with a little water, before slipping the upper part over the same. The best method of dispensing suppositories is undoubtedly in partition paper boxes (see Fig. 278), the sides and bottom of which should be lined with tinfoil

FIG. 278.



Suppository box.

or paraffin paper, the patient always being directed to keep the box in a cool place; in the absence of partitioned boxes, an oblong powder box may be used, the suppositories being placed between two pieces of sheet-wadding.

PART III.

PHARMACEUTICAL CHEMISTRY.

ALTHOUGH the term *pharmaceutical chemistry* is objected to by many who rightfully claim that there can be but one kind of chemistry, the laws and principles of which must be the same whether applied to pharmacy, medicine, physiology, or agriculture, it will, nevertheless, be retained in this book as a convenient heading under which to group the many details of composition, preparation, and examination of that vast number of chemical compounds in almost daily use by pharmacists, and the majority of which are officially recognized in the U. S. Pharmacopœia. The classification of chemical compounds with regard to constitution, etc., will, in the main, not be based upon the views at present accepted by chemists, concerning which the student of pharmacy receives ample instruction in his chemical lectures, and of which he can find full explanation in the many excellent chemical text-books of to-day; but a somewhat unsystematic arrangement will be followed, having in view more particularly the study of official and other chemicals from a pharmaceutical standpoint, irrespective of their chemical relationship. After an experience of many years this plan, being still found the most desirable for pharmacists, is adhered to in pharmaceutical schools.

Chemical compounds may be conveniently divided into those usually designated as inorganic substances and those formerly known as organic compounds, but to which, now, the name carbon compounds is more appropriately applied.

Inorganic Substances.

Of the thirteen elements which are known as non-metallic bodies, all but four are of pharmaceutical interest, either because they are employed extensively by physicians in their elementary state or because they form certain important compounds with each other which are officially recognized in the Pharmacopœia; such compounds only will be considered here, and these are furnished by the following elements: hydrogen, oxygen, chlorine, bromine, iodine, sulphur, phosphorus, carbon, and boron. A very valuable class of com-

pounds formed by these elements are the inorganic acids, which will be treated in a special chapter.

Combinations of non-metallic elements with the metals are very properly classified as compounds of the latter, and will be treated in connection with the salts and numerous other preparations of the metals, officially recognized. The compounds of metals may be conveniently considered according to a system of division which groups those metals together the oxides of which possess certain well-recognized properties in common; thus, metals of the alkalies, of the alkaline earths, of the earths and heavy metals.

Since very few metallic salts are prepared by pharmacists, such compounds will be treated chiefly with a view of enabling the student to understand fully the official requirements as regards identity and quality, detailed consideration being given mainly to those compounds for the preparation of which the Pharmacopœia gives official working formulas.

CHAPTER XXXVI.

HYDROGEN AND OXYGEN.

NEITHER of these elements is of pharmaceutical value in its uncombined gaseous state, but they unite to form two very important compounds.

The most important compound of hydrogen and oxygen is water, which may be looked upon chemically as hydrogen monoxide, H_2O, and has already been referred to on page 206. The Pharmacopœia recognizes both natural and distilled water, and, while in some localities, natural water may be obtained remarkably free from impurities, the use of distilled water is to be preferred at the dispensing counter and for the preparation of aromatic waters and many chemical solutions. Distilled water is required to be absolutely free from both inorganic and organic impurities, while the official limit of the former in natural water is indicated by a residue not exceeding 0.5 Gm. of inorganic salts upon evaporation of 1000 Cc. of water. Natural water mixed with 10 per cent. of its volume of diluted sulphuric acid and ½ per cent. of deci-normal potassium permanganate solution, should not become completely decolorized by boiling it for 10 minutes, showing the pharmacopœial limit of organic and other oxidizable matters.

Hydrogen dioxide, H_2O_2, first obtained in 1818 by Thenard, contains 94 per cent. of oxygen, and is the richest oxygen compound known. It is officially recognized, in the form of a 3 per cent. aqueous solution, under the name Aqua Hydrogenii Dioxidi.

The compound H_2O_2 may be obtained from any metallic dioxide which yields a portion of its oxygen to water, upon treatment with an acid. For technical purposes sodium dioxide is extensively employed, but this method is not suitable for medicinal purposes, as the resulting solution cannot be freed from the accompanying sodium sulphate or chloride; hence the Pharmacopœia directs that the official solution shall be made from barium dioxide, which, upon saturation with an acid, readily gives up one-half of its oxygen to water to form hydrogen dioxide.

An important step in the official process is the thorough hydration of the barium dioxide, in order to insure rapid and complete saturation subsequently with the acid; experience has shown that cold favors the hydration of the finely powdered barium dioxide, which is known to be completed when the water separates but slightly from the resulting magma. Phosphoric acid has been found to produce a better yield of H_2O_2 than sulphuric or carbonic acid, and is

even preferable to hydrochloric acid, owing to the practical difficulty of removing the free acid after decomposition of the barium chloride formed. Hydrofluoric acid has also been successfully employed for the liberation of hydrogen dioxide, but its corrosive nature presents great obstacles to its use, although the resulting barium fluoride is even more insoluble than the phosphate. The hydrated barium dioxide must be fully decomposed, and saturated with acid to exact neutrality; hence the Pharmacopœia directs that a portion of the well-cooled diluted phosphoric acid be set aside as a reserve, and used, in small quantities, after all the barium dioxide mixture has been added to the remainder of the acid, until a perfectly neutral reaction is obtained. Vigorous agitation and refrigeration of the acid and barium mixture are necessary to insure a full yield of H_2O_2. The addition of small quantities of diluted sulphuric acid to the filtered solution is for the purpose of freeing it entirely from barium, a small portion of which will have entered into solution as acid barium phosphate; the subsequent removal of the finely precipitated barium sulphate is greatly facilitated by the admixture of a little starch before filtration. The finished product contains a small amount of phosphoric acid, liberated from the acid phosphate, which materially aids in the preservation of the solution; a trace of sulphuric acid is also present, as it is impossible to avoid adding a slight excess.

Solution of hydrogen dioxide readily undergoes spontaneous decomposition, particularly if exposed to heat and sunlight; it should, therefore, be preserved in a cool, dark place, or in amber-colored bottles, which have been loosely stoppered to avoid explosion in case of defective bottles and increased pressure caused by accumulation of gas. As a preservative, boro-glycerin has been suggested, and, when used in the proportion of 1 part in 100 of the solution, has been found serviceable in retarding the rate of decomposition. Moderate heat is far less injurious than daylight, and Dr. Squibb has found that, if a temperature of 60° C. (140° F.) be not exceeded, a fifty-volume solution can readily be obtained by concentration on a water-bath, without appreciable loss of dioxide; above this temperature, however, decomposition rapidly increases.

The Pharmacopœia requires that solution of hydrogen dioxide shall contain 3 per cent. by weight of the pure dioxide, which corresponds to about 10 volumes of available oxygen. The assay is made with potassium permanganate, in the presence of sulphuric acid, according to the reaction $5H_2O_2 + 3H_2SO_4 + 2KMnO_4 = K_2SO_4 + 2MnSO_4 + 8H_2O + 5O_2$. Only one-half of the oxygen indicated in the equation is derived from the hydrogen dioxide, the other half being furnished by the potassium permanganate, which fact must be considered if the gas is collected and measured in a gas-tube over mercury. The term available oxygen refers, therefore, to the volume of nascent oxygen obtained directly from the dioxide, and not to the total volume liberated in the reaction. From the above equation it

is seen that two molecules (315.34 parts) of potassium permanganate correspond to five molecules (169.60 parts) of hydrogen dioxide; hence each Cc. of a decinormal solution of the former containing 0.0031534 Gm. of $KMnO_4$ must be equivalent to 0.001696 Gm. of H_2O_2, or 0.000798 Gm. of oxygen available therefrom.

Thus the volume strength of any solution of hydrogen dioxide can be conveniently calculated, simultaneously with the percentage strength, without the necessity of collecting and measuring the actual gas volume, by reckoning the weight of one cubic centimeter of oxygen at 0° C. and 760 Mm. atmospheric pressure as equivalent to 0.00143 Gm. (actually 0.001424488); then, dividing the weight of oxygen equivalent to 1 Cc. of $\frac{N}{10}$ $KMnO_4$ solution by 0.00143, we shall obtain 0.56 Cc. (actually 0.5594) as the volume of oxygen represented by each cubic centimeter, and multiplying the number of Cc. $\frac{N}{10}$ $KMnO_4$ solution decolorized by 1 Cc. of H_2O_2 solution by 0.56, the volumes of available oxygen are indicated by the product. Multiplying, at the same time, the number of Cc. $\frac{N}{10}$ $KMnO_4$ solution so decolorized by 0.17 (actually $0.1696 = 0.001696 \times 100$) will yield the percentage by weight of absolute H_2O_2.

The reaction with potassium chromate and ether mentioned in the Pharmacopœia depends upon the formation of a new compound which forms a blue solution with ether; it is characteristic of hydrogen dioxide. By some the compound formed is considered to be perchromic anhydride (Cr_2O_7), a substance analogous to permanganic anhydride (Mn_2O_7), while others assume that it may possibly be a compound of CrO_3 and H_2O_2.

CHAPTER XXXVII.

CHLORINE, BROMINE, AND IODINE.

CHLORINE is used by physicians, in its elementary state, in the form of an aqueous solution, which the Pharmacopœia recognizes under the name of Aqua Chlori, and for the preparation of which an official formula is given.

When manganese dioxide is treated with hydrochloric acid the oxygen which is liberated does not unite with water to form hydrogen dioxide, as in the case of barium and sodium dioxides, but unites with the hydrogen of the hydrochloric acid to form water; the chlorine being thus set free, a portion combines with the manganese, while the remainder passes off in gaseous form, according to the following equation: $MnO_2 + 4HCl = MnCl_2 + Cl_2 + 2H_2O$. The manganese dioxide used should be free from fine particles, in pieces of about the size of small filberts, and used in such quantity that it is not completely covered by the acid liquid; this insures a slow but regular disengagement of chlorine gas and diminishes the loss of acid vapors. Chlorine may also be conveniently evolved from a mixture of sodium chloride, manganese dioxide, and sulphuric acid somewhat diluted with water, sodium chloride yielding over 60 per cent. of its weight of chlorine, the reaction being the following: $2NaCl + MnO_2 + 2\,H_2SO_4 = Na_2SO_4 + MnSO_4 + 2H_2O + Cl_2$.

Since cold favors the solution of gases in water, it is desirable that the water into which the chlorine is conducted be kept at a temperature not above 10° C. (50° F.), at which temperature water absorbs about three times its volume of chlorine gas. The receiving vessel should be shaken from time to time, *as long as absorption takes place*, which is shown by the stopper being drawn in after agitation, in order that a saturated solution may be obtained. The washing of the gas, directed in the official process, is for the purpose of eliminating any hydrochloric acid vapor which may have passed over with the chlorine.

When preparing chlorine water, sulphurous acid, and similar solutions it may happen that, owing to cessation or interruption of the gas-flow, a partial vacuum is produced in the generating flask, and, as a consequence, liquid from the wash-bottle is drawn over into the flask, and, coming in contact with the heated glass, will cause a fracture. This may be avoided either by using a safety-tube or by disconnecting the flask from the wash-bottle as soon as gas-bubbles cease to pass over.

Chlorine water is very unstable, and must be preserved in small,

completely-filled vials, securely stoppered and paraffined, in a cool dark place, otherwise chlorine will escape and the formation of hydrochloric acid rapidly set in. It is one of those preparations requiring the pharmacist's special attention, for, when prescribed by physicians, it is wanted of full strength, which is not possible if the solution be carelessly preserved in partly-filled bottles or exposed to daylight.

The strength of chlorine water, required by the Pharmacopœia to be $\frac{4}{10}$ of 1 per cent. by weight of chlorine, can be ascertained by decomposing a solution of potassium iodide by means of the chlorine water and volumetrically determining the amount of iodine thus set free. Chlorine always displaces iodine in atomic proportions, and, in the official assay the following reaction takes place: $2KI + Cl_2 = 2KCl + I_2$, 70.74 parts of chlorine liberating 253.06 parts of iodine; therefore, 17.7 Gm. of chlorine water, containing 0.0708 Gm. of chlorine (0.4 per cent. of 17.7), would liberate 0.25306 Gm. of iodine, which is held in solution by an excess of potassium iodide. The actual amount of iodine set free is determined with $\frac{N}{10}$ sodium thiosulphate solution, of which each Cc. will decolorize 0.012653 Gm. of iodine in solution, according to the following reaction: $2(Na_2S_2O_3 + 5H_2O) + I_2 = 2NaI + Na_2S_4O_6 + 10H_2O$, sodium iodide and tetrathionate being formed, which both yield colorless solutions. Since 253.06 Gm. of iodine are equal to 70.74 Gm. of chlorine, each Cc. of the $\frac{N}{10}$ sodium thiosulphate solution will represent 0.003537 Gm. of chlorine, and the number of Cc. necessary to decolorize the deep-red liquid may be multiplied by 0.003537 to find the total amount of chlorine present—this multiplied by 100 and divided by the weight of chlorine water used indicates the percentage of chlorine.

Bromine is employed in its free state as an antiseptic and disinfectant, and is occasionally used internally as an alterative. It is a heavy, dark brownish-red liquid, which, even at ordinary temperatures, evolves highly irritating vapor; hence considerable care is necessary in handling bromine. A vial of bromine should be well cooled before opening, especially in warm weather, to avoid accidents, and, if large quantities are to be used, as in the manufacture of syrup of ferrous bromide and similar preparations, it is best to open the vial of bromine under ice water. Contact of bromine or its vapor with metallic surfaces must be carefully avoided.

The manufacture of bromine has rapidly increased during the last thirty years, and immense quantities of it are now produced in this country. It occurs in nature, in aqueous solution, combined with sodium, magnesium, and calcium, and is present in sea-water to the extent of about $\frac{1}{175}$ of 1 per cent. The commercial sources of bromine are the mother-liquors left after the crystallization of sodium chloride at the salt wells of Ohio, Pennsylvania, West Virginia, and Michigan in this country, and near Stassfurt, in Germany. Since the bromides are far more soluble than the chlorides,

the former remain in solution in the mother-liquors, to which the name bittern is given in this country. The bittern is concentrated until a density of about 1.45 is reached, which facilitates the further removal of chlorides and sulphates, then transferred to stone-ware stills, where a mixture of sulphuric acid and manganese dioxide is added, which, with the aid of heat, liberates the bromine according to the following reaction: $MgBr_2 + MnO_2 + 2H_2SO_4 = Br_2 + MgSO_4 + MnSO_4 + 2H_2O$. The bromine vapor is condensed in well-cooled receivers and freed from water by distillation over calcium chloride.

It is difficult to obtain bromine entirely free from chlorine, the plan usually followed being distillation with a bromide, whereby the corresponding chloride is formed and bromine set free. The Pharmacopœia permits the presence of 3 per cent. of chlorine, an excess being indicated by the formation of a precipitate, within three minutes, upon addition of nitric acid to the filtrate obtained after precipitation of 1 Cc. of saturated bromine water with 5 Cc. $\frac{N}{10}$ silver nitrate solution in the presence of 3 Cc. of ammonium carbonate test-solution. This test depends upon the ready solubility of silver chloride and the sparing solubility of silver bromide in ammonium carbonate solution, and is approximately accurate. It has been observed that, if 1 per cent. of chlorine be present, the addition of nitric acid causes only a faint opalescence, but no precipitate, even in one hour's time; 2 per cent. leaves the liquid perfectly transparent, but a white sediment is formed in thirty minutes; 3 per cent. causes separation of white flocculi in three minutes, although the liquid remains transparent, while 4 per cent. causes turbidity and the immediate formation of a flocculent precipitate. To determine the exact amount of chlorine present, the best plan is to mix 1 Gm. of bromine with 10 Cc. of distilled water, adding sufficient ammonia water to produce a clear solution, then digest with barium carbonate, filter, evaporate the filtrate to dryness, and gently ignite the saline residue. The latter should be soluble in absolute alcohol, and every 0.0294 Gm. of insoluble residue will indicate 1 per cent. of chlorine, barium chloride being insoluble, while the bromide is soluble in absolute alcohol.

Bromoform and other organic impurities, which, in part at least, are derived from the luting and fastenings of the stills, may be present in bromine. Iodine is rarely present, but, if so, will be liberated by ferric chloride, if the latter be added to a solution of bromine previously shaken with reduced iron until nearly colorless, and may be detected with the aid of starch; the reaction is as follows: $FeI_2 + Fe_2Cl_6 = 3FeCl_2 + I_2$.

Bromine has been found an efficient antidote to the poison of the rattlesnake, and the following formula for *Bibron's Antidote* is taken from Parrish's *Pharmacy*, published in 1884: Dissolve 5 drachms (300 grains) of bromine in 6 fluidounces of diluted alcohol and 4 grains of potassium iodide and 2 grains of mercuric chloride in 1½

fluidounces of diluted alcohol; mix the two solutions. Dose: 10 drops in a tablespoonful of brandy, to be repeated as required.

IODINE is more extensively employed in its elementary state than any other element, both internally and externally. It was formerly derived solely from the ashes of sea-plants, particularly of certain species of Laminaria. These ashes are known on the coast of Scotland, where at one time the chief iodine manufactories were located, as *kelp*, in Norway as *varec*, and in Spain as *barilla;* they contain iodine in the form of alkali iodides, NaI and KI. After treatment with water, the chlorides, carbonates, and sulphates present are removed by evaporation of the solution and crystallization, sulphuric acid is then added to decompose sulphides and other sulphur compounds; to the acid liquid, manganese dioxide is added, and the mixture is heated. The iodine, volatilizing, passes into suitable condensing flasks and sublimes, a reaction similar to that stated under chlorine and bromine taking place.

At present vast quantities of iodine are obtained in South America, from the mother-liquors of the so-called Chili saltpetre, sodium nitrate, which contains iodine in the form of sodium iodate. The iodine is obtained either by direct precipitation with sodium bisulphite and sulphur dioxide or by sublimation, after addition of manganese dioxide and sulphuric acid to cuprous iodide, which has been previously precipitated from a solution of sodium iodide by cupric and ferrous sulphates. The chemical reactions involved in these two processes can be seen from the following equations:

By direct precipitation:

$$2NaIO_3 + 4NaHSO_3 + SO_2 = 4NaHSO_4 + Na_2SO_4 + I_2.$$

By sublimination, from cuprous iodide:

1. $NaIO_3 + 3NaHSO_3 = 3NaHSO_4 + NaI.$
2. $2NaI + 2CuSO_4 + 2FeSO_4 = Cu_2I_2 + Na_2SO_4 + Fe_2(SO_4)_3.$
3. $Cu_2I_2 + 2MnO_2 + 4H_2SO_4 = 2CuSO_4 + 2MnSO_4 + I_2 + 4H_2O.$

The crude iodine thus obtained is freed from moisture and purified by resublimation. Commercial iodine may contain, as impurities, cyanogen, chlorine, and bromine, present as CNI, ICl_3, and IBr. The Pharmacopœia demands the absence of iodine cyanide, which is a very poisonous compound, and limits the amount of chlorine and bromine. In the official test for iodine cyanide, a further addition of a drop of ferric chloride test-solution, made before adding the sodium hydroxide solution, would render the reaction much sharper, as it depends upon the formation of ferric ferrocyanide, $Fe_4(FeC_6N_6)_3$, which, if present in sufficient quantity, will settle as a blue precipitate, otherwise only a blue color is imparted to the liquid. The official limit-test for chlorine and bromine depends upon the greater solubility of silver chloride and bromide in ammonia water and their subsequent precipitation upon the addition of nitric acid.

The Pharmacopœia requires 98.85 per cent. purity in iodine, which

is volumetrically determined with $\frac{N}{10}$ sodium thiosulphate solution, each Cc. of which corresponds to 0.012653 Gm. of iodine. If 0.32 Gm. of iodine be used for the valuation, as directed in the Pharmacopœia, 25 Cc. of the $\frac{N}{10}$ $Na_2S_2O_3$ solution will be required to decolorize the liquid completely; for 98.85 per cent. of 0.32 is equal to 0.31632, and 0.31632 divided by 0.012653 yields 25. The reaction involved in this test has already been explained under chlorine.

One solid and two liquid preparations containing iodine in a free state are recognized in the Pharmacopœia, namely, an alcoholic tincture containing 7 Gm. of iodine in 100 Cc.; an aqueous solution known as Lugol's solution, containing 5 per cent., by weight, of iodine held in solution by twice its weight of potassium iodide; and an ointment containing 4 per cent., by weight, of iodine. The amount of iodine present in any sample of the tincture or compound solution can be readily determined by titration with sodium thiosulphate, as directed in the Pharmacopœia the addition of potassium iodide, in the valuation of tincture of iodine, is for the purpose of preventing the precipitation of iodine by the water.

In the *National Formulary* three other liquid preparations of iodine are mentioned: Churchill's tincture of iodine, Churchill's iodine caustic, and decolorized tincture of iodine. The first two named should not be confounded with each other, as they differ greatly in strength, the tincture being of about one-half the strength of the caustic. Decolorized tincture of iodine is not a solution of iodine at all, the name being misapplied; the finished colorless product contains sodium iodide, sodium tetrathionate, and ammonium iodide formed by reaction between iodine, sodium thiosulphate, and ammonia water. The preparation, in a short time, takes on a disagreeable alliaceous odor and deposits crystals of sodium tetrathionate, which may be removed by filtration.

Iodine forms with hydrogen an important although rather unstable compound, hydriodic acid, HI, which is the active ingredient in an official syrup of that name. The acid can be obtained by bringing iodine in contact with hydrogen sulphide, but is preferably made by decomposition of an alkali iodide by tartaric acid. In the official formula for the syrup the following reaction, yielding hydriodic acid, takes place: $KI + H_2C_4H_4O_6 = HI + KHC_4H_4O_6$, the resulting acid potassium tartrate being removed partly by using a hydroalcoholic solvent and partly by exposing the mixture to cold. 165.56 parts of potassium iodide yield 127.53 parts of hydriodic acid; hence the 13 Gm. used in the official formula should yield 10 Gm., or sufficient to make 1000 Gm. of syrup of the required strength, 1 per cent. by weight. The potassium hypophosphite ordered in the Pharmacopœia is added to preserve the acid solution, for, if any iodine should be liberated, the following reaction would take place: $KH_2PO_2 + 2I_2 + 2H_2O = 3HI + KI + H_3PO_4$, the syrup thus being restored to its original condition. In all probability there are traces of free hypophosphorous acid present in the syrup prepared

according to the Pharmacopœia, since 12 Gm. of tartaric acid are used, of which only 11.75 + Gm. are required for the potassium iodide; for complete decomposition of the hypophosphite, 1.44 Gm. of tartaric acid would be necessary.

The valuation of syrup of hydriodic acid, made by means of $\frac{N}{10}$ silver nitrate solution, depends upon the following reaction: $HI + AgNO_3 = AgI + HNO_3$, 127.53 parts of the acid requiring 169.55 parts of the silver salt for complete precipitation; hence each Cc. of the decinormal solution containing 0.016955 Gm. of $AgNO_3$ represents 0.012753 Gm. of HI. Potassium chromate is used to indicate the end of the reaction, by forming red silver chromate as soon as the hydriodic acid has all been precipitated as silver iodide; silver chromate, however, is soluble in acid and alkaline liquids, and ammonia water is therefore added to the syrup to exact neutrality, so as to prevent the liberation of nitric acid which would interfere with the precipitation of the silver chromate and thus vitiate the end reaction. This neutralization in no wise interferes with the valuation, the reactions taking place as follows:

1. $HI + NH_4OH = NH_4I + H_2O$.
2. $NH_4I + AgNO_3 = AgI + NH_4NO_3$.

CHAPTER XXXVIII.

SULPHUR, PHOSPHORUS, CARBON, AND BORON.

SULPHUR is found widely diffused, both in the free state and in combination. While by far the greater portion of sulphur used in this country comes from Italy, it is now also successfully mined in the States of California, Nevada, and Utah, a bed of sulphur 2000 feet square and over 60 feet thick existing in the latter State. Commercially, sulphur occurs in four varieties, namely, that known as stick or roll sulphur, chiefly used for fumigation and bleaching; and sublimed, washed, and precipitated sulphur, extensively used in medicine. Roll sulphur, also known as brimstone, is prepared by heating the crude sulphur obtained from various sources, allowing impurities to settle and pouring the fused sulphur into cylindrical moulds in which it is allowed to congeal.

Sublimed Sulphur, as its name indicates, is obtained by vaporizing sulphur and passing the vapor into large stone or brick chambers, the temperature of which is not allowed to rise above 100° or 110° C. (212° or 230° F.), where the sulphur is deposited in partly crystalline and partly amorphous particles known as flowers of sulphur. The two varieties can be separated from each other by treatment with carbon disulphide, which dissolves the amorphous but not the crystalline sulphur. In boiling solutions of alkali hydroxides, sulphur is perfectly soluble, forming such compounds as alkali pentasulphide and thiosulphate. Nearly all sulphur is contaminated with arsenic and this, as arsenic tersulphide, As_2S_3, together with traces of selenium and some sulphuric acid formed by oxidation, are the usual impurities found in sublimed sulphur. Not more than one-half per cent. of fixed impurities should remain upon ignition.

Washed Sulphur is recognized in the Pharmacopœia as Sulphur Lotum and is prepared by digesting sublimed sulphur with diluted ammonia water. This treatment removes any sulphuric acid and arsenic sulphide present as ammonium sulphate, arsenite, and sulpharsenite, according to the following reaction: $H_2SO_4 + As_2S_3 + 8NH_4OH = (NH_4)_2SO_4 + (NH_4)_3AsO_3 + (NH_4)_3AsS_3 + 5H_2O$. The mixture is subsequently strained and the resulting purified sulphur is washed with cold water to remove excess of ammonia. In the official test for the absence of arsenic, the latter substance would unite with ammonia, as above stated, and be precipitated as As_2S_3, upon addition of hydrochloric acid. Since traces of selenium are sometimes present, the Pharmacopœia gives a special test for the same, which depends upon the formation of potassio-selenium cyanide,

KSeCN; this is decomposed subsequently by hydrochloric acid, separating selenium, which imparts a reddish color to the liquid. Washed sulphur should be protected against a damp atmosphere, otherwise slow oxidation sets in and an acid reaction becomes perceptible.

Precipitated Sulphur, also known as lac sulphuris or milk of sulphur, is made from sublimed sulphur by first uniting this to an alkali and then decomposing the resulting compound with an acid. Milk of lime is preferred mainly on account of its cheapness; upon boiling it with sulphur, both pentasulphide and thiosulphate are obtained in solution, thus: $12S + 3CaO = 2CaS_5 + CaS_2O_3$. The Pharmacopœia directs that hydrochloric acid shall be added to the clear filtrate until the latter is nearly neutralized, but still exhibits an alkaline reaction; this is partly to avoid decomposition of the calcium thiosulphate, which would yield sulphur insoluble in carbon disulphide and in a coarser state of division, and partly to prevent the precipitation of any arsenic trisulphide, for, if arsenic had been present in the sublimed sulphur, it would have formed calcium sulpharsenate, $Ca_3As_2S_8$, which is soluble in the alkaline liquid, but is decomposed by acids. The official process causes a decreased yield of precipitated sulphur, but a purer product, the final reaction being only between the calcium pentasulphide and hydrochloric acid. Sulphuric acid is sometimes used in place of hydrochloric acid, but is not permissible, since it would contaminate the sulphur with insoluble calcium sulphate, whereas hydrochloric acid yields calcium chloride, easily removable by washing.

Sulphur forms two compounds with iodine, a monoiodide, S_2I_2, and a hexiodide, SI_6; only the former is of interest to pharmacists, as it is sometimes used by physicians in the form of an ointment. The official directions for making sulphur iodide are very simple, and, as union of the two elements takes place at a moderately elevated temperature, loss of iodine can be easily avoided. The compound must be preserved in well-stoppered vials, as it readily decomposes when exposed to the air; the union is not a very strong one, as boiling water is capable of abstracting all the iodine from it.

PHOSPHORUS occurs in nature chiefly as calcium phosphate which makes up the structure of bone and is found as extensive mineral deposits. Pure phosphorus is obtained by distilling calcium metaphosphate with sand and charcoal. Owing to its great avidity for oxygen and ready inflammability, it must be preserved under water and care is necessary in handling it. Elementary phosphorus is used to a considerable extent in medicine, entering into the composition of four official preparations, the elixir, oil, pill, and spirit of phosphorus; all but the second named have already been considered in previous chapters, on pages 234, 240, and 332, where also special precautions regarding the weighing of small quantities of phosphorus have been given.

Phosphorated Oil, or Oleum Phosphoratum of the Pharmacopœia, contains 1 per cent. of phosphorus, about 90 per cent. of expressed oil

of almond, and about 10 per cent. of ether, all by weight. When the oil is heated to 250° C. (482° F.) for fifteen minutes, air and moisture are first expelled and afterward certain organic matters are volatilized, the oil becoming colorless; upon cooling, flocculi are deposited, which are removed by filtration. The addition of ether materially aids in the preservation of the solution. Each gramme of phosphorated oil represents 10 milligrammes of phosphorus, which is equal to about ½ grain in every fluidrachm.

CARBON is recognized, in the Pharmacopœia, in the form of wood charcoal and animal charcoal; the former will be considered in connection with the products of woody fibre (see Cellulose). Animal charcoal is extensively employed as a decolorizing agent by manufacturing chemists; it is prepared by roasting bone in iron cylinders until vapors cease to be given off; the residuary charcoal mixed with large proportions of inorganic constituents is known in its crude state as bone-black. Meat and blood are also made to yield animal charcoal by a somewhat similar process. Purified animal charcoal differs from crude bone-black in having been repeatedly treated with boiling diluted hydrochloric acid, whereby all acid soluble impurities, such as calcium carbonate and phosphate, are removed. By this treatment, animal charcoal loses about 80 per cent. in weight, leaving a small proportion (4 per cent.) of siliceous matter mixed with the purified charcoal. If not completely carbonized, animal charcoal will impart color to water if boiled with the same in the presence of potassium hydroxide. The remarkable decolorizing property of animal charcoal is due to the very fine state of division of the carbon and its consequent increased surface attraction. While crude animal charcoal is largely used for neutral solutions in the arts, only the purified article can be employed for acid liquids or delicate chemical solutions. So-called spent charcoal, charged with organic matter, can be regenerated by appropriate heating.

The only preparation of carbon to be considered is carbon disulphide, CS_2, which is not employed medicinally, but is a valuable solvent for caoutchouc, fats, and many other substances. It is prepared by direct union of charcoal and sulphur, vapors of the latter being passed over the former, heated to redness, and then condensed in suitable receivers. It is freed from dissolved sulphur by distillation on a water-bath, while hydrogen sulphide, which is also formed, is removed by agitation with mercury; the liquid is further rectified by distillation with wax or fat, whereby certain offensive sulphur compounds are removed. When exposed to light, carbon disulphide assumes a yellow color and develops a fetid odor, owing to decomposition. The Pharmacopœia demands the absence of dissolved sulphur, hydrogen sulphide, and sulphur dioxide.

BORON is never used in pharmacy or medicine in its free state. Its compound with oxygen, boric acid, will be considered in the next chapter.

CHAPTER XXXIX.

THE INORGANIC ACIDS.

THE different combinations of hydrogen, as well as of hydrogen and oxygen, with other non-metallic elements, yield a class of compounds known as inorganic acids, which, being extensively employed, are of great importance to the pharmacist. The presence of hydrogen, whether it has been introduced in its elementary state or in the form of water, lends to these compounds their peculiar acid character. Compounds with oxygen only, possess no acid properties and are termed anhydrides or simply oxides; they, however, will unite chemically with water to form well-defined acids; thus we have sulphurous and sulphuric anhydrides, SO_2 and SO_3, known also as sulphur dioxide and trioxide, which, combining with water, yield sulphurous and sulphuric acids, as $SO_2 + H_2O = H_2SO_3$ and $SO_3 + H_2O = H_2SO_4$; carbon dioxide, CO_2, in contact with water, yields carbonic acid, H_2CO_3; nitric anhydride, or nitrogen pentoxide, N_2O_5, yields nitric acid, HNO_3, thus $N_2O_5 + H_2O = 2HNO_3$; phosphoric anhydride or phosphorus pentoxide, P_2O_5, will yield with water phosphoric acid, H_3PO_4, thus $P_2O_5 + 3H_2O = 2H_3PO_4$, etc.

Acids, as is well known, are characterized by a sour taste, the property of changing the color of blue litmus paper to red, of neutralizing alkalies, and of forming with these and other bases well-defined salts. The salts thus formed are not always neutral compounds, which fact is due to different basicity of the various acids, depending upon the number of replaceable hydrogen atoms present in the acid; hence the terms mono-, di-, tri-, and tetrabasic, referring to the presence of 1, 2, 3, or 4 atoms of hydrogen, which can be replaced by as many basylous atoms or groups, giving rise to normal and acid salts. Normal salts are such as are formed by complete saturation of an acid by a base, or, in other words, they are produced whenever all the replaceable hydrogen of an acid is replaced by a base; acid salts, on the other hand, still retain a part of the replaceable hydrogen of acids, and are the result of imperfect neutralization of an acid by a base. (Examples, KNO_3 and Na_2SO_4 are normal salts, while $NaHCO_3$ and KH_2PO_4 are acid salts.) Monobasic acids can never form acid salts. In the pharmacopœial chemical formulas for acids the replaceable hydrogen is stated first, hence the basicity of the acid can be seen at a glance; thus hydrochloric, hydrobromic, hypophosphorous, and nitric acids are all monobasic, sulphurous and sulphuric acids are dibasic, while boric and phosphoric acids are tribasic.

Both crude and purified acids are offered for sale by manufacturers; the former, while suitable for many technical purposes, should never be used for pharmaceutical preparations. A very important point in connection with inorganic acids is the percentage of absolute acid present in the commercial solutions sold under their respective names. The Pharmacopœia, in every instance, designates the percentage strength of the official acids, and pharmacists should insist on being furnished such acids by manufacturing chemists; the designation C. P. (chemically pure), placed on the labels of acid bottles, is no clue as to the strength of the solution; either the initials U. S. P. or the percentage of absolute acid should be stated. Manufacturing chemists will not be slow in recognizing the justice of such a demand, if pharmacists insist upon it; otherwise, the same uncertainty as to strength will continue. All working formulas of the Pharmacopœia, requiring the use of inorganic acids, are based upon the assumption that acids of official strength will be used. Absolute purity is not demanded for official acids, for, while this is essential for chemical reagents, it is considered unnecessary for medicinal acids, and, if insisted upon, would greatly enhance the cost of the article without improving the acid for medicinal or pharmaceutical purposes. Certain impurities, which it would be difficult to remove entirely, except at considerable expense, are allowed by the Pharmacopœia to be present within prescribed limits. As different acids have different saturating powers, the official volumetric determinations are only useful in fixing the strength of the acid examined, after the absence of other acids has been proved by the tests prescribed for that purpose.

Only such inorganic acids will be considered here as are designated in the Pharmacopœia, and are therefore of special interest to the student of pharmacy. Details of the manufacture of the leading acids will not be essayed, as the text-books on chemistry furnish all such information. While there must naturally exist a great diversity in the strength of the various so-called strong acids, the Pharmacopœia has fixed the proportion of absolute acid in all official diluted inorganic acids at 10 per cent., with the exception of diluted nitro-hydrochloric acid. With one exception, boric acid, all the official inorganic acids are liquid, although the Pharmacopœia also designates as acids two compounds, arsenic trioxide and chromium trioxide, which will be considered elsewhere.

The following is a list of the official inorganic acids: Boric Acid, Diluted Hydrobromic Acid, Hydrochloric Acid, Diluted Hydrochloric Acid, Diluted Hypophosphorous Acid, Nitric Acid, Diluted Nitric Acid, Nitrohydrochloric Acid, Diluted Nitrohydrochloric Acid, Phosphoric Acid, Diluted Phosphoric Acid, Sulphuric Acid, Aromatic Sulphuric Acid, Diluted Sulphuric Acid, Sulphurous Acid.

Boric Acid. H_3BO_3 or $B(OH)_3$. Boric acid occurs in nature both in a free and combined state, the free acid, in the form of

vapor, issuing with steam from the earth in volcanic regions, particularly in Tuscany, Italy, while the combined acid is usually found as sodium tetraborate or borax. Medicinal boric acid is probably all obtained by decomposition of a boiling solution of borax with hydrochloric acid, which latter is preferable to sulphuric acid, as it can be more readily removed by washing from the crystals of boric acid; the reaction is a very simple one—$(Na_2B_4O_7 + 10H_2O) + 2HCl = 4H_3BO_3 + 2NaCl + 5H_2O$. When heated, boric acid gradually loses water and is converted into metaboric acid, HBO_2, with increasing temperature, into tetraboric, $H_2B_4O_7$, and, finally, above 160° C. (320° F.) all hydrogen is eliminated in the form of water and boron trioxide remains; thus $2H_3BO_3 = B_2O_3 + 3H_2O$.

The Pharmacopœia requires the absence of all impurities in boric acid except traces of iron. Its chief characteristics are that it imparts a green color to the flame of burning alcohol, and that it changes the yellow color of turmeric paper brown even in the presence of hydrochloric acid.

Diluted Hydrobromic Acid. An aqueous solution containing 10 per cent. by weight of absolute HBr. Pure hydrobromic acid is a gaseous compound, and is rather unstable. The medicinal acid is prepared, by manufacturers, usually of two strengths, 34 per cent. and 10 per cent., the former being the more economical article to purchase, as the requisite proportion of water to reduce it to the official acid can be easily added by the pharmacist, 10 Gm. of 34 per cent. acid mixed with 24 Gm. of distilled water yielding 34 Gm. of 10 per cent. acid. Hydrobromic acid can be obtained in several ways, but is usually made, on a large scale, by a method first suggested by Dr. Squibb. Moderately diluted sulphuric acid is poured slowly, and with constant stirring, into a hot saturated solution of potassium bromide, when the following decomposition takes place: $2KBr + H_2SO_4 = 2HBr + K_2SO_4$; after twenty-four hours the potassium sulphate has crystallized out, the solution of hydrobromic acid is poured off, and the crystals are slowly washed with ice-cold water to recover any adhering acid. Finally, the acid liquid is distilled in a glass retort, on a sand-bath, nearly to dryness. Its strength is ascertained by titration with normal potassium hydroxide solution, and sufficient water added to produce either a 34 or 10 per cent. solution as desired.

For preparing small quantities of the official acid, the precipitation method of Wade and Fothergill may be employed, which is based on the decomposition of potassium bromide with tartaric acid; thus $KBr + H_2C_4H_4O_6 = HBr + KHC_4H_4O_6$. 11.9 Gm. of potassium bromide and 15 Gm. of tartaric acid are each dissolved in 30 Cc. of cold distilled water; the acid solution is poured into the saline solution, and the mixture, after having been well shaken for five or ten minutes, is placed in ice-water or an ice-chest for twenty-four or thirty-six hours; it is then filtered, and the vessel and filter carefully

washed with ice-cold water until the filtered liquid weighs 81 Gm. A small quantity of acid potassium tartrate is apt to remain in the diluted acid prepared by this method.

The Pharmacopœia excludes all impurities except slight traces of arsenic, and directs that 8.08 Gm. of the official diluted acid shall require 10 Cc. of $\frac{N}{1}$ KOH solution for neutralization. According to the equation, $KOH + HBr = KBr + H_2O$, each Cc. of $\frac{N}{1}$ KOH solution containing 0.05599 Gm. of KOH corresponds to 0.08076 Gm. HBr, and 10 Cc. would correspond to 0.8076 Gm., which is practically 10 per cent. of 8.08 Gm. The official acid has a specific gravity of about 1.077 at 15° C. (59° F.).

Hydrochloric Acid. This acid may be prepared quite pure by decomposing sodium chloride with pure sulphuric acid and conducting the gas into water. The crude acid of commerce is often obtained, as a by-product, in the manufacture of sodium or potassium carbonates from the respective chlorides; since sulphates are first made in this process by acting on the chlorides with sulphuric acid, the reactions are the same in the manufacture of crude and pure acid, and possibly occur in two distinct steps, namely: 1. $NaCl + H_2SO_4 = HCl + NaHSO_4$. 2. $NaCl + NaHSO_4 = HCl + Na_2SO_4$. The crude acid of commerce is often of a deep yellow color, owing to organic matter and traces of iron in solution; it should not be employed for pharmaceutical preparations.

Official hydrochloric acid should be free from all impurities, except a bare trace of non-volatile substances and arsenic, the latter derived in all probability from the sulphuric acid. It has a specific gravity of about 1.163 at 15° C. (59° F.), and should contain 31.89 per cent. by weight of absolute HCl, which is determined by titration with $\frac{N}{1}$ KOH solution. The Pharmacopœia directs the use of 3.64 Gm. for the assay, which, at 31.89 per cent., should contain 1.1608 Gm. of HCl. Since each Cc. of $\frac{N}{1}$ KOH solution corresponds to 0.0364 Gm. of HCl, the 3.64 Gm. of acid will require 31.9 Cc. of $\frac{N}{1}$ KOH solution for complete neutralization, for 1.1608 divided by 0.0364 yields 31.89+.

Strong hydrochloric acid, when exposed to the air, usually produces white fumes, due partly to the moisture in the air and partly to the ammonia more or less present, ammonium chloride being formed.

Diluted Hydrochloric Acid is made from the official acid by mixing it with distilled water, in the proportion of 10 parts of the former to 21.9 parts of the latter, by weight, or, as the Pharmacopœia gives it, 100 Gm. of the acid with 219 Gm. of distilled water. This must yield a liquid containing 10 per cent. of absolute HCl, for the 100 Gm. of official hydrochloric acid contain 31.89 per cent. of HCl, and 31.89 Gm. is equal to 10 per cent. of 319 Gm. Diluted hydrochloric acid has a specific gravity of about 1.050 at 15° C. (59° F.),

and corresponds in all its properties, reactions, and tests to the official stronger acid, except that it is odorless and produces no fumes when exposed to the air, and that 3.64 Gm. require only 10 Cc. of $\frac{N}{1}$ KOH solution for neutralization.

DILUTED HYPOPHOSPHOROUS ACID. Hypophosphorous acid is a strong reducing agent used in pharmacy chiefly to prevent oxidation of certain unstable solutions, such as those of hydriodic acid. It can be obtained by decomposition of any of the soluble hypophosphites with an acid yielding an insoluble compound. The National Formulary directs the use of potassium hypophosphite and tartaric acid, when the following reaction occurs: $KH_2PO_2 + H_2C_4H_4O_6 = HH_2PO_2 + KHC_4H_4O_6$, the newly formed acid potassium tartrate being removed both by the use of a hydro-alcoholic solvent and cold. Calcium hypophosphite and oxalic acid have also been employed with excellent results, 69 parts of the former requiring 50.4 parts of the latter, and the reaction occurring thus: $Ca(H_2PO_2)_2 + H_2C_2O_4 = 2HH_2PO_2 + CaC_2O_4$. The official acid contains 10 per cent. of absolute HH_2PO_2, and has a specific gravity of about 1.046 at 15° C. (59° F.), but, for manufacturing purposes, a 50 per cent. acid is also on the market. Traces of phosphoric, oxalic, and tartaric acids, as also of potassium, are permitted, as indicated in the official tests. The strength of the acid may be determined by both its neutralizing and its reducing powers, the latter being the more reliable, however, although the two tests may be used to corroborate each other. The reaction between hypophosphorous acid and potassium permanganate takes place according to the following equation: $5HH_2PO_2 + 6H_2SO_4 + 4KMnO_4 = 5H_3PO_4 + 2K_2SO_4 + 4MnSO_4 + 6H_2O$; hence each Cc. of $\frac{N}{10}$ $KMnO_4$ solution corresponds to 0.001647 Gm. of absolute HH_2PO_2. In the pharmacopœial test, 0.5 Gm. of diluted hypophosphorous acid is used, which, as seen above, would require 30.3 Cc. of $\frac{N}{10}$ $KMnO_4$ solution for complete oxidation, known by the appearance of a permanent pink tint; it has been found more convenient, however, to add at once an excess of the $KMnO_4$ solution, and determine the actual excess by retitration with oxalic acid, which involves a further reaction, thus: $5(H_2C_2O_4 + 2H_2O) + 3H_2SO_4 + 2KMnO_4 = 10CO_2 + K_2SO_4 + 2MnSO_4 + 18H_2O$. As each Cc. of decinormal oxalic acid solution corresponds in value exactly to 1 Cc. of decinormal potassium permanganate solution, simple subtraction of the number of Cc. necessary to discharge the purple color will indicate the actual number of Cc. of $\frac{N}{10}$ $KMnO_4$ solution reduced by the sample of hypophosphorous acid used, and this multiplied by 0.001647 gives the total amount of HH_2PO_2 present; from these figures the percentage can be readily calculated.

NITRIC ACID. When potassium or sodium nitrate is treated with sulphuric acid, nitric acid is liberated, and may be condensed in

suitable receivers. The reaction, in the case of potassium nitrate, occurs as follows: $KNO_3 + H_2SO_4 = HNO_3 + KHSO_4$; in the case of Chili saltpetre, provided a sufficient quantity of sodium nitrate be used, two distinct reactions may be said to occur, namely: 1. $NaNO_3 + H_2SO_4 = HNO_3 + NaHSO_4$; 2. $NaHSO_4 + NaNO_3 = HNO_3 + Na_2SO_4$. Sodium nitrate affords a larger yield than potassium nitrate, since the acid sodium sulphate reacts with the undecomposed nitrate at a much lower temperature than the acid potassium sulphate, the latter requiring a temperature at which the nitric acid is apt to be decomposed.

The Pharmacopœia demands absolute purity for nitric acid. If exposed to sunlight, the acid soon undergoes decomposition, a red color being imparted to the liquid, due to the formation of nitrogen tetroxide, N_2O_4, hence the acid must be kept in a dark place. Nitric acid of different strengths is placed upon the market by manufacturing chemists, ranging from 1.21 to 1.50 specific gravity, hence care is necessary to obtain the only kind recognized by the Pharmacopœia, which contains 68 per cent. of absolute HNO_3 and has a specific gravity of 1.414 at 15° C. (59° F.), otherwise considerable annoyance may be experienced when nitric acid is to be used as an oxidizing agent in any of the official preparations.

Nitric acid, being the most corrosive of the official acids, requires care in handling; in contact with the skin, it acts chemically on the same and produces a deep yellow stain, this behavior, characteristic of nitric acid with albuminoid substances, being known as the xanthoproteic reaction.

Each Cc. of $\frac{N}{1}$ KOH solution will represent 0.06289 Gm. of absolute HNO_3, nitric acid being monobasic, and 34 Cc. will, therefore, be necessary to neutralize 3.145 Gm. of the official acid, for 68 per cent. of 3.145 is 2.1386, and 2.1386 divided by 0.06289 yields 34.

The so called nitrous acid of commerce is simply nitroso-nitric acid, that is, nitric acid containing variable amounts of nitrogen tetroxide.

Diluted Nitric Acid is made by diluting official nitric acid with distilled water in the proportion of 100 Gm. of the former to 580 Gm. of the latter, and must, therefore, contain 10 per cent. of absolute HNO_3. 100 Gm. of official acid containing 68 Gm., which are equal to 10 per cent. of 680 Gm., the total weight of the finished product. It has a specific gravity of about 1.057 at 15° C. (59° F.), and 6.29 Gm. should require 10 Cc. of $\frac{N}{1}$ KOH solution for complete neutralization.

Nitrohydrochloric Acid. This preparation, which is also known as nitromuriatic acid, is not of a definite chemical composition, but is considered by physicians a valuable remedial agent. When strong nitric and hydrochloric acids are brought into contact, mutual decomposition takes place, the composition of the finished

product depending upon the proportions of the acids used and the temperature at which they have been mixed. The Pharmacopœia directs 18 volumes of nitric acid and 82 volumes of hydrochloric acid, and, when so mixed, the following reactions probably take place: $HNO_3 + 3HCl = NOCl + Cl_2 + 2H_2O$ and $2HNO_3 + 6HCl = 2NOCl_2 + Cl_2 + 4H_2O$, nitrosyl mono- and dichloride and water being formed, while chlorine is liberated. The mixture is at first colorless, but, as reaction progresses, an orange-red color is developed and effervescence is observed; the liberated gas is very irritating, hence the operation should be conducted in a cool place, in the open air or under a flue. This preparation should never be made extemporaneously, as severe accidents may result from such a proceeding; sufficient time must be allowed for complete reaction, which is known by cessation of effervescence, after which the liquid, which has assumed a green-yellow color, should be preserved in dark, glass-stoppered bottles, in a cool place. Nitrohydrochloric acid must never be dispensed in completely filled bottles, and the patient should be cautioned against keeping it in a warm room. The acid is also known as chloro-nitrous acid and aqua regia, and owes its power of dissolving gold to the free chlorine and feeble chlorine compounds present.

Diluted Nitrohydrochloric Acid is of nearly one-fourth the strength of the stronger acid, 22.5 per cent., and is prepared in exactly the same manner, the diluent, distilled water, not being added until all effervescence has ceased. The British Pharmacopœia prepares this acid by mixing the stronger acids at once with the water and setting the mixture aside for fourteen days. Conflicting views exist regarding the composition of the finished product, some authorities contending that, when made by diluting the strong acids at once with water, the same reactions will occur as in a mixture of the acids alone, except that the decomposition is more gradual, while others assert that little or no change will take place, and that, in fact, the decomposed strong acids will be again restored to their original condition upon the addition of water, nitric and hydrochloric acids being regenerated. Certain it is that the diluted nitrohydrochloric acid differs from the strong acid in being free from color and possessing only a faint odor of chlorine when freshly made, which is gradually lost. The author has never observed any effervescence or change of color or odor upon mixing the strong acids direct with water and allowing the mixture to stand.

Phosphoric Acid. The official acid is a dense syrupy liquid containing 85 per cent. of absolute orthophosphoric acid, H_3PO_4 or $PO(OH)_3$, and has a specific gravity of 1.710 at 15° C. (59° F.). Medicinal phosphoric acid should all be made direct from phosphorus; usually oxidation by means of nitric acid is resorted to, each part of phosphorus requiring about 3½ parts of absolute nitric acid

for complete conversion, according to the following equation: $5HNO_3 + P_3 + 2H_2O = 3H_3PO_4 + 5NO$.

In order to control the reaction, about an equal weight of water is mixed with a portion of the nitric acid contained in a flask, the phosphorus is added, and the whole heated on a water-bath; when the reaction slackens, the balance of the nitric acid is added, undiluted, small portions at a time, and the heat is continued until all the phosphorus is dissolved, after which the liquid is heated in a porcelain dish, on a sand-bath, at a temperature not exceeding 190° C. (374° F.), until all traces of nitric acid have been removed. The object of limiting the temperature is to avoid conversion of the orthophosphoric acid into pyrophosphoric acid, which occurs at 200° C. (392° F.) and over. Phosphorus is frequently contaminated with arsenic, which is best removed, at this stage of the process, by diluting the acid liquid with water, passing a stream of hydrogen sulphide through it for several hours and afterward setting the liquid aside for twenty-four hours to allow the arsenic sulphide to subside. After filtration, the excess of gas is removed by heating and the liquid evaporated to the desired density, every 100 Gm. of phosphorus used yielding about 370 Gm. of official phosphoric acid. This is essentially the modified process suggested some years ago by Dr. Squibb.

In 1875, Markoe proposed the following process, which has since then been used, with marked success, on a large scale. 900 Gm. of phosphorus are placed in a stone jar and covered with 5400 Gm. of water, after which 10 Gm. of iodine are added and the mixture stirred so as to bring the iodine into contact with the phosphorus. From a glass-stoppered burette or funnel, 60 Gm. of bromine are now added, drop by drop, in such a manner that the bromine shall strike the phosphorus as it falls below the water. Phosphorus pentaiodide and pentabromide, PI_5 and PBr_5, chiefly the latter, are formed by direct union, and, when the reaction has ceased, 5400 Gm. of nitric acid are added, the jar is placed in cold water or surrounded with ice, to control the rate of oxidation, and set aside until solution of the phosphorus has been effected. The acid liquid is then evaporated and treated as above. The phosphorus iodide and bromide are decomposed by the water present, forming phosphoric, hydriodic, and hydrobromic acids; the last two are decomposed by the nitric acid regenerating iodine and bromine with the liberation of nitric oxide. These reactions, continuing until all the phosphorus has been converted into phosphoric acid, may be expressed by the following equations: 1. $PI_5 + 5PBr_5 + 24H_2O = 6H_3PO_4 + 5HI + 25HBr$; 2. $HI + 5HBr + 2HNO_3 = I + 5Br + 2NO + 4H_2O$. The process can be conducted with bromine alone, but the presence of iodine has been found to modify the action between the phosphorus and bromine.

The impurities likely to be met with in phosphoric acid can, as a rule, be avoided in the process of manufacture, phosphorous acid being due to insufficient oxidation, while meta- and pyrophosphoric acids arise from the use of excessive heat.

Phosphoric acid made from phosphorus should be miscible with tincture of ferric chloride in all proportions, but, if made from glacial phosphoric acid, it causes turbidity, which is in part due to the presence of sodium metaphosphate in the glacial acid.

The value of the volumetric assay of phosphoric acid depends largely upon the indicator employed; complete neutralization is not feasible, since the normal alkali phosphate itself gives an alkaline reaction. Phosphoric acid is tribasic, and, therefore, capable of forming three different compounds with the alkalies, namely, KH_2PO_4, K_2HPO_4, and K_3PO_4; the last-named salt is alkaline to all color-indicators, whereas the other two are either acid, alkaline, or neutral to different indicators. With phenolphtalein, KH_2PO_4 shows an acid reaction, but K_2HPO_4 a neutral reaction, but with methyl-orange and Congo-red, KH_2PO_4 already shows a neutral reaction, and K_2HPO_4 an alkaline reaction. Therefore, when phenolphtalein is used as an indicator, as prescribed in the Pharmacopœia, two molecules of potassium hydroxide will be required for every molecule of absolute phosphoric acid to form the salt K_2HPO_4, secondary or dibasic potassium phosphate, according to the equation $H_3PO_4 + 2KOH = K_2HPO_4 + 2H_2O$. Each Cc. of $\frac{N}{1}$ KOH solution, containing 0.05599 Gm. KOH, will indicate 0.0489 Gm. H_3PO_4, when the neutral reaction with phenolphtalein is just passed, which is shown by a permanent pink tint imparted by a drop of the alkali solution. In the official test, at least 17 Cc. of $\frac{N}{1}$ KOH should be required before an alkaline reaction is shown, for 17×0.0489 is equal to 0.8313, and 85 per cent. of 0.978 is 0.8313. With methyl-orange as an indicator, each Cc. of $\frac{N}{1}$ KOH solution represents 0.0978 Gm. H_3PO_4, for an alkaline reaction (a golden-yellow color) will be observed upon the addition of one or two drops in excess of the quantity necessary to form primary or monobasic potassium phosphate, KH_2PO_4, an equal number of molecules of the acid and alkali being concerned in the reaction; thus, $H_3PO_4 + KOH = KH_2PO_4 + H_2O$.

Diluted Phosphoric Acid is made from the preceding acid by dilution with distilled water in the proportion of one part by weight of the strong acid and seven and one-half parts of water, or 100 Gm. and 750 Gm. It contains 10 per cent. of absolute H_3PO_4, and has a specific gravity of about 1.057 at 15° C. (59° F.).

Sulphuric Acid. The manufacture of this acid is carried on extensively in this country and in Europe, in specially constructed factories so arranged that the fumes from burning sulphur or iron pyrites are brought into contact with steam and nitric acid vapor in leaden chambers. Nitrogen trioxide is generated and combines with more sulphur dioxide, aqueous vapor, and atmospheric oxygen, forming nitrosylsulphuric acid, which, coming into contact with water, is decomposed, yielding sulphuric acid and nitrogen trioxide,

and this, in turn, again unites with more sulphur dioxide, etc. The following equations will explain the various steps in the process :

1. $2SO_2 + 2HNO_3 + H_2O = 2H_2SO_4 + N_2O_3$.
2. $N_2O_3 + 2SO_2 + O_2 + H_2O = 2SO_2OHNO_2$.
3. $2SO_2OHNO_2 + H_2O = 2H_2SO_4 + N_2O_3$.

The foregoing are the chief reactions involved in the manufacture of sulphuric acid, which condenses and is dissolved in the water covering the floor of the leaden chambers, thus forming a dilute acid which gradually becomes more concentrated; it is afterward withdrawn, still further concentrated in leaden pans, and finally distilled in glass or, preferably, gold-lined platinum retorts.

Crude sulphuric acid is often colored, and contains nitric and sulphurous acids and lead, the latter being readily detected by simple dilution with water. Arsenic is almost invariably present, and thus is transferred to other substances in the manufacture of which sulphuric acid is used, as hydrochloric and nitric acids, phosphorus, etc.

When sulphuric acid is mixed with water or alcohol, heat is developed and the volume of the mixture is invariably contracted. Official sulphuric acid is of oily consistence, and has a specific gravity of 1.835 at 15° C. (59° F.). It should be free from lead and other mineral impurities, but slight traces of arsenic, nitric, nitrous, and sulphurous acids are permitted. The Pharmacopœia requires the presence of not less than 92.5 per cent. of absolute H_2SO_4, and, as sulphuric acid is bibasic, the following reaction takes place when potassium hydroxide is added to complete neutrality: $H_2SO_4 + 2KOH = K_2SO_4 + 2H_2O$. Each Cc. of $\frac{N}{1}$ KOH solution, containing 0.05599 Gm. KOH, is equivalent to 0.04891 Gm. H_2SO_4.

Aromatic Sulphuric Acid. An alcoholic solution of sulphuric acid, flavored with ginger and cinnamon, containing about 10 per cent. by volume, or nearly 20 per cent. by weight, of official acid. It is a light-colored liquid having a specific gravity of about 0.939 at 15° C. (59° F.). The acid should be added to the alcohol slowly in a thin stream, with constant stirring, and, when the mixture has cooled, the tincture of ginger and oil of cinnamon may be added. Upon standing, chemical action ensues and a part of the sulphuric acid is gradually converted into ethyl-sulphuric or sulphovinic acid, according to the equation $H_2SO_4 + C_2H_5OH = C_2H_5HSO_4 + H_2O$. The new compound, also known as acid ethyl sulphate, is soluble in water and alcohol, but cannot be precipitated by barium chloride; by boiling, it is split up into sulphuric acid and alcohol; hence the Pharmacopœia directs, in the official volumetric test for aromatic sulphuric acid, that the dilute mixture shall be boiled for a few minutes and cooled before titrating it.

The aromatic sulphuric acid of the present Pharmacopœia differs considerably from the preparation of the same name of the 1870

Pharmacopœia, formerly often prescribed under the name of *Elixir of Vitriol.* The latter preparation was of a brownish-red color, and very prone to precipitation; it was made by percolating 1 troy ounce of ginger and 1½ troy ounces of cinnamon with 1 pint of alcohol, and adding the resulting tincture to a previously prepared and cooled mixture of 1 pint of alcohol and 6 troy ounces of sulphuric acid.

DILUTE SULPHURIC ACID is made by diluting 10 parts by weight of official sulphuric acid with 82½ parts of distilled water, or 100 Gm. of the former with 825 Gm. of the latter. The acid should be added gradually, with constant stirring, on account of the heat developed. It contains 10 per cent. of absolute H_2SO_4 and has a specific gravity of about 1.070 at 15° C. (59° F.).

SULPHUROUS ACID. Under this name the Pharmacopœia recognizes an aqueous solution of sulphur dioxide, containing not less than 6.4 per cent. by weight of the gas. The official directions for preparing the solution are explicit, and, if followed, cannot fail to yield a satisfactory product. The charcoal acts as a deoxidizing agent upon the sulphuric acid, sulphur dioxide and carbon dioxide being generated, as shown in the following equation: $4H_2SO_4 + C_2 = 4SO_2 + 2CO_2 + 4H_2O$. Heat is necessary to induce the reaction, and in order to intercept any impurities which may be mechanically carried over with the escaping gases the latter are made to pass through water contained in a wash-bottle. The carbon dioxide will escape from the bottle containing the distilled water as the sulphur dioxide is absorbed, since it is insoluble in a solution of sulphurous acid; it may be retained, however, in the solution of sodium carbonate unless much SO_2 gas should also pass over. The use of the bottle containing sodium carbonate solution can be readily dispensed with if the operation be conducted in the open air or under a flue.

In the place of charcoal, pure copper foil or turnings may be used for the generation of sulphur dioxide; the yield of gas from an equal weight of sulphuric acid, however, will be only one-half of that obtained with charcoal, as may be seen from the equation $4H_2SO_4 + Cu_2 = 2SO_2 + 2CuSO_4 + 4H_2O$, although the evolution of carbon dioxide is avoided; the official process is therefore more economical.

As in the case of chlorine water, the water intended for the absorption of the sulphur dioxide should be kept cold, so as to avoid the loss of gas, and the finished solution must be preserved in small, completely filled, glass-stoppered vials in a cool, dark place, as the sulphurous acid rapidly absorbs oxygen and is converted into sulphuric acid when carelessly exposed, thus losing all its valuable medicinal properties. The precautions regarding fracture of the generating flask, already stated under chlorine water, should also be observed in the case of this solution.

The pharmacopœial test with lead acetate paper depends upon the

reaction between sulphur dioxide and nascent hydrogen (generated from zinc with hydrochloric acid), resulting in the formation of hydrogen sulphide, thus $SO_2 + H_6 = H_2S + 2H_2O$. Slight traces of sulphuric acid are unavoidable, except in freshly made solutions; hence the official limit test.

The strength of sulphurous acid solutions is determined, volumetrically, with iodine as an oxidizing agent, the following reaction taking place: $H_2SO_3(SO_2 + H_2O) + I_2 + H_2O = 2HI + H_2SO_4$, 2 atoms of iodine converting 1 molecule of sulphurous acid into sulphuric acid. Each Cc. of $\frac{N}{10}$ iodine solution, containing 0.012653 Gm. iodine, therefore corresponds to 0.003195 Gm. SO_2, and 2 Gm. of the official acid must require at least 40 Cc., for 6.4 per cent. of 2 is 0.128, and 0.128 divided by 0.003195 yields 40. Starch solution is used to indicate the end of the reaction by striking a blue color with the least excess of iodine added.

CHAPTER XL.

THE COMPOUNDS OF POTASSIUM.

THE Pharmacopœia recognizes seventeen salts of potassium, besides seven preparations of salts, including three liquids, for which working formulas are given; the following comprise the list:

Official English Name.	Official Latin Name.
Potassa,	Potassa.
Potassa with Lime,	Potassa Cum Calce.
Sulphurated Potassa,	Potassa Sulphurata.
Potassium Acetate,	Potassii Acetas
Potassium Bicarbonate,	Potassii Bicarbonas.
Potassium Bichromate,	Potassii Bichromas.
Potassium Bitartrate,	Potassii Bitartras.
Potassium Bromide,	Potassii Bromidum.
Potassium Carbonate,	Potassii Carbonas.
Potassium Chlorate,	Potassii Chloras.
Potassium Citrate,	Potassii Citras.
Effervescent Potassium Citrate,	Potassii Citras Effervescens.
Potassium Cyanide,	Potassii Cyanidum.
Potassium and Sodium Tartrate,	Potassii et Sodii Tartras.
Potassium Ferrocyanide,	Potassii Ferrocyanidum.
Potassium Hypophosphite,	Potassii Hypophosphitum.
Potassium Iodide,	Potassii Iodidum.
Potassium Nitrate,	Potassii Nitras.
Potassium Permanganate,	Potassii Permanganas.
Potassium Sulphate,	Potassii Sulphas.
Solution of Potassa,	Liquor Potassæ
Solution of Potassium Arsenite,	Liquor Potassii Arsenitis.
Solution of Potassium Citrate,	Liquor Potassii Citratis.
Troches of Potassium Chlorate,	Trochisci Potassii Chloratis.

POTASSA. KOH. This compound, better known as caustic potash, is, chemically speaking, potassium hydroxide or hydrate, obtained by decomposing a solution of potassium carbonate with milk of lime, evaporating the clear filtrate in perfectly clean iron or silver vessels until a small quantity of the liquid congeals upon cooling, and then pouring it into cylindrical moulds, whence the sticks are removed while still warm.

The purity of the product obtained depends upon the quality of the potassium carbonate employed, and if made from the bicarbonate it is of much better quality. White caustic potash in sticks, labelled potassa by lime, is the kind generally used for pharmaceutical purposes, and should not contain over 5 or 6 per cent. of moisture; commercial caustic potash is sometimes found to contain as much as 20 or 25 per cent. of water. For chemical purposes potassa is purified by means of alcohol or baryta, being then known as potassa by alcohol or potassa by baryta.

Potassa is a powerful caustic, very deliquescent, and rapidly absorbs carbon dioxide from the air; it must therefore be handled carefully, and preserved in tightly stoppered bottles.

The Pharmacopœia requires that official potassa shall contain at least 90 per cent. of absolute potassium hydroxide, which is ascertained by titration with normal acid, each Cc. of which requires 0.05599 Gm. KOH for neutralization. The official assay, requiring 9 Cc. of $\frac{N}{1}$ H_2SO_4 for 0.56 Gm. of potassa, is only absolutely accurate in the absence of soda, as the latter, having a lower molecular weight, requires a relatively larger quantity of acid for saturation; the small amount of soda permitted will not, however, materially affect the result, and may well be ignored.

With a few exceptions the limits of impurities allowed by the Pharmacopœia, in this and other compounds of potassium, rarely exceed $\frac{1}{2}$ of 1 per cent., and are usually determined volumetrically. Since potassa readily absorbs carbon dioxide, as much as 1.38 per cent. of potassium carbonate is allowed in the official article, as shown by the test with lime-water; 5 Cc. of lime-water, containing about 0.148 per cent., or 0.0074 Gm. of $Ca(OH)_2$, are capable of precipitating 0.0138 Gm. of K_2CO_3, which is equal to 1.38 per cent. of 1 Gm. of the sample.

Besides slight traces of potassium silicate and nitrate, 1.5 per cent. of soda is also permitted in the official potassa, which is indicated by the quantity of normal potassium hydroxide solution necessary to cause an alkaline reaction in the filtrate obtained after precipitating all KOH present in 0.56 Gm. of the sample as acid potassium tartrate, by means of tartaric acid. Any soda present in the potassa will also have been converted into an acid tartrate, but will remain in solution, and, upon the addition of sufficient $\frac{N}{1}$ KOH solution, be converted into normal double tartrate; 0.2 Cc. $\frac{N}{1}$ KOH solution corresponds exactly to 0.008 Gm. NaOH, which is 1.5 per cent. of 0.56 Gm., and the first drop added beyond this point should cause a permanent pink color, if it has not already appeared, showing an excess of alkali.

Potassa with Lime. This preparation is a simple mechanical mixture of equal parts of potassa and lime, intended as a milder application than potassa alone. The object of mixing the ingredients in a warm mortar is to prevent the absorption of moisture, and, as the powder rapidly deteriorates upon exposure to air, it must be kept in tightly stoppered vials. Potassa with lime is also known as Vienna Caustic. It is rarely used.

Sulphurated Potassa, or liver of sulphur, has been known for nearly 500 years, and for over 100 years has been made in the same manner as now officially prescribed. When potassium carbonate and sulphur are heated together, carbon dioxide is evolved and the sulphur unites with the potassium, forming polysulphides, a portion of which

is oxidized to thiosulphate by the oxygen of the carbonate in excess over that passing off as carbon dioxide. Small quantities of potassium sulphate are also possibly formed, and, since high heat favors such a change, the temperature should be so regulated that the mass at no time shall assume a thin fluid condition, and that as little sulphur as possible be consumed. If the preparation is carefully made, the following reaction is likely to occur: $3K_2CO_3 + S_8 = 2K_2S_3 + K_2S_2O_3 + 3CO_2$; but with a higher heat potassium sulphate is formed from the thiosulphate.

Sulphurated potassa is not a definite chemical compound, its composition being variable and depending upon the care used in its manufacture. It must be protected against air and moisture to avoid further oxidation, which is indicated by a change in color from liver-brown to green and finally gray.

The medicinal virtues of sulphurated potassa reside chiefly in the potassium sulphides present, the Pharmacopœia demanding at least 12.85 per cent. of sulphur in such combination, which may be determined by treatment with crystallized cupric sulphate. The following equation, $CuSO_45H_2O + K_2S_3 = CuS + S_2 + K_2SO_4 + 5H_2O$, shows that 248.8 parts of cryst. cupric sulphate require 31.98 parts of sulphur for complete precipitation of the copper; hence 1 Gm., as prescribed in the official test, will require 0.1285 Gm. of sulphur, which is equivalent to 12.85 per cent. of the weight of sulphurated potassa used.

Potassium Acetate. $KC_2H_3O_2$. This salt is prepared by neutralizing acetic acid with potassium carbonate or bicarbonate, the latter being preferable on account of its greater purity, evaporating the resulting solution to dryness, fusing the residue, and allowing the salt to solidify. The product, being very deliquescent, must be bottled while still warm, and should be well protected against air.

The salt absorbs moisture very quickly when in contact with air, which it is impossible to prevent while weighing, hence only 98 per cent. of acetate is officially demanded.

In order to determine the quality of organic salts of potassium volumetrically, it is necessary that they be first converted into carbonate by thorough ignition, the oxygen of the atmosphere aiding in the change. In the case of potassium acetate the following reaction occurs: $2\,KC_2H_3O_2 + O_8 = K_2CO_3 + 3H_2O + 3CO_2$, two molecules, or 196 parts, of acetate furnishing one molecule, or 138 parts, of carbonate; each Cc. of $\frac{N}{1}$ H_2SO_4 therefore required to neutralize the resulting carbonate in the official test represents 0.098 Gm., or 10 per cent. of acetate; for 138 : 196 :: 0.069 : 0.098.

Potassium Bicarbonate. $KHCO_3$. When carbon dioxide is passed into a concentrated solution of potassium carbonate, chemical union takes place, potassium bicarbonate or acid carbonate being formed according to the equation, $K_2CO_3 + H_2O + CO_2 = 2\,KHCO_3$.

The solution is afterward decanted from any separated silica, and crystallized. Potassium bicarbonate is permanent in the air, any hygroscopic tendency indicating contamination with carbonate; this can be verified by adding to a solution of the salt barium chloride or magnesium sulphate, which are not precipitated by the pure bicarbonate. The Pharmacopœia admits slight traces of carbonate and chloride, also of iron.

POTASSIUM BICHROMATE, more properly DICHROMATE. $K_2Cr_2O_7$. Although the official title of bichromate has been retained in the Pharmacopœia, this is not in conformity with the chemical composition of the salt. The term bichromate, according to accepted usage, would indicate a monobasic acid salt, requiring the formula $KHCrO_4$, a salt not known, whereas the official salt has the composition $K_2Cr_2O_7$, showing it to be a compound of dichromic acid, $H_2Cr_2O_7$. This acid may be looked upon as obtained by the union of two molecules of chromic acid with the elimination of water; thus, $H_2CrO_4 + H_2CrO_4 = H_2Cr_2O_7 + H_2O$; or it may be assumed that chromic anhydride is capable of forming both chromic and dichromic acids; thus, $CrO_3 + H_2O = H_2CrO_4$ and $2\ CrO_3 + H_2O = H_2Cr_2O_7$. Dichromic acid may be said to be chromic acid holding chromic trioxide in solution, and is analogous to disulphuric, or fuming sulphuric, acid.

Potassium dichromate is obtained by treating a solution of the chromate with sulphuric acid—thus, $2\ K_2CrO_4 + H_2SO_4 = K_2Cr_2O_7 + K_2SO_4 + H_2O$—and separating the resulting salts by crystallization. The chromate is obtained direct from chrome-iron ore, $FeOCr_2O_3$, by roasting the same, in reverberatory furnaces, with potassium carbonate and chalk, the latter simply preventing fusion of the mixture, which is finally treated with water and strained to remove the iron.

POTASSIUM BITARTRATE. $KHC_4H_4O_6$. Acid potassium tartrate, or cream of tartar, as it is more familiarly known, is prepared for medicinal use by treating purified tartar with diluted hydrochloric acid for the purpose of removing the calcium tartrate present as chloride; the mixture is heated and constantly agitated while cooling. Some tartaric acid and potassium bitartrate remain subsequently in the mother-liquors, which are utilized in the manufacture of tartaric acid.

Crude tartar, or argol, is obtained as a natural deposit in wine-casks, during the fermentation of grape-juice, and is purified by repeated treatment with water, clay, and animal charcoal to remove coloring-matters and other substances; the filtered solution is crystallized, the resulting product still containing 5 to 15 per cent. of calcium tartrate as an impurity, which remains.

The Pharmacopœia permits a very slight admixture of calcium tartrate, less than 1 per cent., in the official article, but demands at least 99 per cent. of true acid potassium tartrate, which is determined

by conversion into carbonate by means of ignition, as in the case of potassium acetate, and then titrating with normal acid. The following equations show that 376 Gm. of potassium bitartrate yield 138 Gm. of the carbonate, and that therefore each Cc. of $\frac{N}{1}$ H_2SO_4 must correspond to 0.18767 Gm. $KHC_4H_4O_6 : 2KHC_4H_4O_6 + O_{10} = K_2CO_3 + 7Co_2 + 5H_2O$ and $K_2CO_3 + H_2SO_4 = K_2SO_4 + CO_2 + H_2O$.

While the second issue of the United States Pharmacopœia for 1890 directs the foregoing method of valuation for potassium bitartrate, the first edition directed the assay to be made by titration of the free acid present with $\frac{N}{1}$ KOH solution, each Cc. of which is capable of neutralizing 0.07482 Gm. of tartaric acid, and must therefore correspond to 0.18767 Gm. of true potassium bitartrate, because each molecule, or 149.64 Gm. of tartaric acid will yield one molecule, or 187.67 Gm., of the bitartrate, a mono-basic acid salt, which has one-half the saturating power of the pure acid.

Much of the cream of tartar sold is of inferior quality and often largely adulterated, but there is no difficulty in procuring the official article if it is desired, as it is extensively manufactured in this country and abroad.

The so-called soluble cream of tartar, or boro-tartrate of potassium and sodium, is officially recognized in the German Pharmacopœia under the name *tartarus boraxatus*. It is soluble in its own weight of cold water, and is prepared by digesting 5 parts of potassium bitartrate in a solution of 2 parts of borax and 15 parts of water until dissolved; the solution is evaporated to dryness, and the residue, while still warm, reduced to powder.

Potassium Bromide. KBr. This well-known salt may be obtained by decomposing a solution of ferrous bromide with potassium carbonate, heating the mixture, filtering, evaporating the filtrate, and crystallizing. The process followed by large manufacturers is to add bromine to a solution of potassa until the liquid remains colored, evaporate it to dryness, and expose the saline residue, mixed with charcoal, in small portions at a time, to a red heat in an iron crucible; the fused mass is treated with water, the resulting solution filtered and set aside to crystallize. When bromine and potassa are brought together, potassium bromide and bromate are formed; thus, $6KOH + Br_6 = 5KBr + KBrO_3 + 3H_2O$; by heating the mixed salts with charcoal all bromate is reduced to bromide; thus, $KBrO_3 + C_3 = KBr + 3CO$.

The chief impurity likely to be encountered in potassium bromide is the chloride due to the chlorine present in bromine. The Pharmacopœia demands the absence of more than 3 per cent. of chloride, which is ascertained volumetrically with decinormal silver nitrate solution. Since potassium chloride has a lower molecular weight (74.40) than the bromide (118.79), an equal weight of the same will

require a larger amount of silver solution for complete precipitation; upon this the official test is based.

The following rule will enable anyone to ascertain the exact percentage of potassium chloride in any sample of bromide: Calculate how much $\frac{N}{10}$ $AgNO_3$ solution will be required to precipitate a given weight of pure potassium bromide, and find also the quantity necessary to precipitate the same weight of pure potassium chloride. (Assuming that 0.5 Gm. of each salt be taken, it will require 42.09 Cc. of the silver solution for the bromide, and 67.2 Cc. for the chloride.) Subtract the lesser amount from the greater ($67.2 - 42.09 = 25.11$), and the remainder will represent the difference for 100 per cent., or absolute purity. If this remainder be divided by 100 ($25.11 \div 100 = 0.2511$), the quotient will represent the quantity of $\frac{N}{10}$ $AgNO_3$ solution necessary to indicate 1 per cent. Divide the quotient so obtained into the difference between the quantity of $\frac{N}{10}$ $AgNO_3$ solution required for the given weight of a sample of bromide and for the same weight of pure bromide, the result will indicate the percentage of chloride in the sample.

When potassium chromate is used as an indicator, no permanent red color, due to silver chromate, can appear in the official test until all bromide and chloride have been precipitated. Applying the above rule to the quantities of potassium bromide and silver solution prescribed by the Pharmacopœia, 3 per cent. of chloride will be found indicated, as can be shown by the following calculations: 1 Cc. of $\frac{N}{10}$ $AgNO_3$ solution represents 0.011879 Gm. KBr or 0.00744 Gm. KCl; for 169.55 parts of silver nitrate will completely precipitate 118.79 parts of potassium bromide, or 74.4 parts of potassium chloride; therefore 0.5 Gm. KBr, if absolutely pure, will require 42.09 Cc. of $\frac{N}{10}$ $AgNO_3$ solution—for $0.5 \div 0.011879 = 42.09$, and 0.5 Gm. KCl, if pure, require 67.20 Cc. of $\frac{N}{10}$ $AgNO_3$ solution—for $0.5 \div 0.00744 = 67.20$; $67.20 - 42.09 = 25.11$, and $25.11 \div 100 = 0.2511$. Every 0.2511 Cc. of the silver solution used in excess of 42.09 Cc. for complete precipitation of 0.5 Gm. of potassium bromide will indicate 1 per cent. of chloride; now, $42.85 - 42.09 = 0.76$, and $0.76 \div 0.2511 = 3$.

Potassium Carbonate. K_2CO_3. This compound is familiarly known as salt of tartar, a name given to it because it was at one time prepared by ignition of tartar. It is now extensively prepared from potassium chloride by a method analogous to the Leblanc process for making sodium carbonate. The purer carbonate, such as is demanded by the Pharmacopœia, is obtained by heating crystallized potassium bicarbonate to redness, whereby carbon dioxide and water are eliminated and potassium carbonate remains, the yield being about 68 or 69 per cent. The reaction is a very simple one, $2KHCO_3 = K_2CO_3 + CO_2 + H_2O$.

Potassium carbonate, on account of its very deliquescent nature, must be preserved in well-stoppered bottles, in a dry place. The

Pharmacopœia demands an almost absolutely pure salt, 95 per cent. of potassium carbonate being required and only slight traces of potassium chloride and iron permitted; 3 to 4 per cent. of moisture is usually present.

POTASSIUM CHLORATE. $KClO_3$. At present potassium chlorate is probably chiefly made by a process similar to that given in the British Pharmacopœia, which consists in passing chlorine gas into a moist mixture of potassium carbonate and slaked lime; more water is subsequently added, the mixture boiled for a short time, and set aside to crystallize. The product is purified by recrystallization. The first reaction produces calcium hypochlorite and chloride, the former being decomposed by heat into chlorate and chloride; calcium chlorate then reacts with potassium carbonate, forming potassium chlorate and calcium carbonate. Leaving out the intermediate products, the reaction may be expressed as follows: $K_2CO_3 + 6Ca(OH)_2 + Cl_{12} = 2KClO_3 + 5CaCl_2 + CaCO_3 + 6H_2O$.

Potassium chlorate is rarely found impure, and occurs in commerce both in the form of crystals and fine powder; two varieties are met with—the British and French. It is readily decomposed, often with explosive violence, when triturated with such substances as sugar, tannin, sulphur, etc.; care is therefore necessary when such mixtures are to be dispensed. (See also page 356.)

POTASSIUM CITRATE. $K_3C_6H_5O_7 + H_2O$. This salt is prepared by neutralizing a solution of citric acid with potassium carbonate or bicarbonate, and evaporating the solution to dryness, with constant stirring, so as to obtain the salt in small granules. The finished product retains a little over $5\frac{1}{2}$ per cent. of water, but should be free from impurities; the commercial article is frequently acid, showing imperfect saturation. As the salt is deliquescent, it must be well protected against air.

In order to determine the quality of potassium citrate volumetrically, it is necessary to convert the salt into carbonate by ignition, and then to titrate with normal acid, as in the case of other organic potassium salts. Citric acid being tribasic, two molecules, or 648 parts, of potassium citrate will yield three molecules, or 414 parts of carbonate; thus $2K_3C_6H_5O_7H_2O + O_{18} = 3K_2CO_3 + 9CO_2 + 7H_2O$; therefore, 1.08 Gm. ordered in the official test should yield 0.69 Gm. K_2CO_3, requiring 10 Cc. $\frac{N}{1}$ H_2SO_4.

EFFERVESCENT POTASSIUM CITRATE. The proportions of citric acid and potassium bicarbonate directed in the official formula for this preparation are exactly right for forming a neutral citrate, as shown by the equation, $H_3C_6H_5O_7H_2O + 3KHCO_3 = K_3C_6H_5O_7 + 3CO_2 + 4H_2O$. Owing to the small amount of water of crystallization present in the citric acid, a slight reaction occurs upon triturating the substances together, a pasty mass resulting, but complete

reaction is not intended to take place until the finished preparation is dissolved in water. The prescribed temperature must not be exceeded in drying the mass, so as to avoid fusion, coloration, and loss of carbon dioxide. It should be preserved in tightly stoppered bottles, in a dry place.

POTASSIUM CYANIDE. KCN or KCy. This very poisonous compound is prepared on a large scale by exposing to red heat a mixture of dried potassium ferrocyanide and pure potassium carbonate, whereby potassium cyanide and cyanate are formed, carbon dioxide is eliminated, and metallic iron is precipitated; the fused white mass is carefully decanted and allowed to solidify. The following equation explains the reaction which takes place: $2K_4FeCy_6 + 2K_2CO_3 = 10KCy + 2KCyO + Fe_2 + 2CO_2$. Potassium cyanate may be removed by means of alcohol or carbon disulphide.

A purer product may be obtained by passing hydrocyanic acid gas into an alcoholic solution of potassa, when the newly formed cyanide will separate as a bulky crystalline precipitate, which may be washed on a filter with alcohol.

In the official volumetric determination of potassium cyanide, advantage is taken of the formation of a soluble double cyanide of silver and potassium to indicate when one-half of the cyanogen present in a sample of potassium cyanide has combined with silver; hence, when a permanent precipitate of silver cyanide first appears, double the value is assigned to the silver solution used which it would possess if all the potassium cyanide were decomposed and precipitated. In the official test each Cc. of $\frac{N}{10}$ $AgNO_3$ solution represents 0.013002 Gm. KCy, according to the equation, $2KCy + AgNO_3 = AgK(Cy)_2 + KNO_3$; as soon as this point is passed, the following reaction occurs upon the addition of more silver solution, and a permanent precipitate appears: $AgK(Cy)_2 + AgNO_3 = 2AgCy + KNO_3$. The Pharmacopœia demands that the official salt shall contain 90 per cent. of pure KCy.

POTASSIUM AND SODIUM TARTRATE. $KNaC_4H_4O_6 + 4H_2O$. This salt is commercially known as Rochelle Salt from the fact that it was first obtained at Rochelle, France, by an apothecary named Seignette, over two hundred years ago. It is prepared by neutralizing the free acid in cream of tartar with sodium carbonate, whereby a normal double tartrate is produced; the solution, which must be neutral, is boiled for a short time, filtered, concentrated, and set aside to crystallize, the crystals being afterward pulverized. According to the following equation, $2KHC_4H_4O_6 + (Na_2CO_3 + 10H_2O) = 2(KNaC_4H_4O_6\ 4H_2O) + CO_2 + 3H_2O$, 8 parts of official cream of tartar will require about 6 parts of crystallized pure sodium carbonate, yielding about 12 parts of crystallized Rochelle salt.

Potassium and sodium tartrate is recognized in the British Phar-

macopœia by the name of *soda tartarata*, and in the German Pharmacopœia as *tartarus natronatus;* it is also known as *sal Seignetti.*

Absolute purity is demanded for this salt by the Pharmacopœia, which is determined by conversion into carbonate and titration with normal acid. Each molecule of potassium and sodium tartrate yields one molecule of the double carbonate, upon thorough ignition, as shown by the equation, $KNaC_4H_4O_6 4H_2O + O_8 = KNaCO_3 + 3CO_2 + 6H_2O$; hence 1 Cc. $\frac{N}{1}$ H_2SO_4 represents 0.141 Gm. of the crystallized salt.

Potassium Ferrocyanide. $K_4Fe(CN)_6 + 3H_2O$. Yellow prussiate of potash possesses no medicinal properties, but is the source of official hydrocyanic acid and other cyanides; when pure the salt is not poisonous. It is made by heating, in iron vessels, with constant stirring, a mixture of potassium carbonate, metallic iron, and scraps of horn, leather, or other nitrogen-bearing substances. The fused mass, known as "melt," is, after cooling, leached with water, and the solution decanted and crystallized; the insoluble residue consists of iron, charcoal, ferrous sulphide, calcium phosphate, and silica.

When chlorine is passed into a solution of potassium ferrocyanide, the ferricyanide, or red prussiate of potash, a valuable chemical reagent, is produced, as shown by the following equation, $2K_4Fe(CN)_6 + Cl_2 = K_6Fe_2(CN)_{12}$ or $2K_3Fe(CN)_6 + 2KCl$.

Potassium Hypophosphite. KH_2PO_2. Although this salt can be made by boiling phosphorus with solution of potassa, it is preferably obtained by adding potassium carbonate to a solution of calcium hypophosphite, when calcium carbonate will be precipitated and potassium hypophosphite remain in solution, which can be recovered by filtering the mixture and carefully evaporating the filtrate on a water-bath, with constant stirring, until a granular salt results. The following equation shows the decomposition: $Ca(H_2PO_2)_2 + K_2CO_3 = 2KH_2PO_2 + CaCO_3$.

Potassium hypophosphite is very deliquescent, and must be preserved in tightly stoppered bottles; as it readily explodes when intimately mixed with oxidizing agents, trituration with such substances must be avoided.

The official salt is required to contain at least 98.7 per cent. of pure KH_2PO_2, which is ascertained by titration with decinormal potassium permanganate solution in excess, and retitration of the excess with oxalic acid, as already explained under diluted hypophosphorous acid. The equation, $5KH_2PO_2 + 6H_2SO_4 + 4KMnO_4 = 5KH_2PO_4 + 2K_2SO_4 + 4MnSO_4 + 6H_2O$, shows that each Cc. of $\frac{N}{10}$ $KMnO_4$ solution represents 0.0025977 Gm. KH_2PO_2; hence if 38 Cc. (40–2) are required for 0.1 Gm. of the salt, it must contain 98.7 per cent. of the pure hypophosphite, for $38 \times 0.0025977 = 0.0987126$, which is 98.7 per cent. of 0.1.

POTASSIUM IODIDE. KI. When iodine is added to a solution of potassa the two substances combine, forming potassium iodide and iodate; thus, $6KOH + I_6 = 5KI + KIO_3 + 3H_2O$. The process of manufacturing this salt is analogous to that given for potassium bromide, the iodate being reduced to iodide by heating with charcoal.

Much of the commercial potassium iodide does not respond to the requirements of the Pharmacopœia, as it occurs in white opaque crystals, which, having been obtained from an alkaline solution, are less pure; the official requirements demand practically total absence of alkali, and such a salt crystallizes in colorless transparent cubes, but can also be obtained in the form of a white, granular powder. The pharmacopœial test for the presence of potassium cyanide (due to cyanogen derived from the iodine) involves the formation of potassium ferrocyanide, which, reacting with ferrous sulphate, rapidly produces a blue color, owing to the oxidizing effect of the air. Since each Cc. of $\frac{N}{10}$ $AgNO_3$ solution represents 0.016556 Gm. KI, 0.5 Gm. of an absolutely pure salt will require 30.25 Cc. for complete precipitation; if more than this quantity be required, it would indicate the presence of bromide or chloride. The Pharmacopœia requires at least 99.5 per cent. of pure iodide, and hence states that 0.5 Gm. shall require not less than 30 nor more than 30.25 Cc. of decinormal silver-nitrate solution.

POTASSIUM NITRATE. KNO_3. The sources of this salt were at one time chiefly the natural deposits in India and extensive plantations in Europe and elsewhere for the artificial production of potassium nitrate by putrefaction of animal and vegetable matter in the presence of wood-ashes and calcareous earth. It is now largely obtained by mutual decomposition of potassium chloride and native sodium nitrate, advantage being taken of the lesser solubility of the newly formed sodium chloride to rid the solution of this impurity upon concentration by boiling. The potassium nitrate subsequently crystallizes out, and is further purified by re-solution and re-crystallization.

Potassium nitrate is to be had both in the form of large crystals and as a fine granular powder; the latter is preferred for pharmaceutical purposes, and is largely obtained from the manufacturers of gunpowder, who require a pure article for their purposes.

The name saltpetre, or nitre, is used almost exclusively in commerce, for this salt, and when fused and cast into round moulds it is sold under the name *sal prunelle*.

POTASSIUM PERMANGANATE. $KMnO_4$. In the manufacture of this compound the first step necessary is the production of potassium manganate, by heating to semi-fusion at a dull, red heat, an intimate mixture of manganese dioxide, caustic potassa, and potassium chlorate, when the following reaction occurs: $3MnO_2 + 6KOH$

$+KClO_3=3K_2MnO_4+KCl+3H_2O$. The green, fused mass is then twice treated with boiling water, whereby the potassium manganate is converted into permanganate—$3K_2MnO_4 + 2H_2O = 2KMnO_4 + MnO_2 + 4KOH$—manganese dioxide being again precipitated and potassium hydroxide remaining in solution with the permanganate. The presence of potassa in the liquid prevents a full yield of permanganate by holding a portion of the manganate in solution without change; a stream of carbon dioxide is therefore passed into the liquid to neutralize the potassa and thus allow all the manganate to be converted into permanganate and dioxide; in place of carbon dioxide, diluted sulphuric acid is sometimes used for the same purpose. Finally, after decantation and filtration through asbestos, the solution is concentrated and set aside to crystallize. As potassium permanganate is readily decomposed by organic matter, all dust and dirt must be excluded during the last steps of the process.

The official method of valuation of potassium permanganate, by means of oxalic acid, depends upon the ready deoxidation of the salt by all reducing substances, two and one-half atoms of oxygen being liberated from each molecule of the permanganate. In the official test the oxalic acid is completely converted by oxidation into carbon dioxide and water, as shown by the following equation: $5(H_2C_2O_4+2H_2O)+2KMnO_4+3H_2SO_4=10CO_2+K_2SO_4+2MnSO_4+18H_2O$, 628.5 parts of crystallized oxalic acid requiring 315.34 parts of pure permanganate. The Pharmacopœia demands potassium permanganate to be of 98.7 per cent. purity, 0.1 Gm. of which will oxidize 0.196717 Gm. of oxalic acid; or, in other words, 0.196717 Gm. of crystallized acid will be required to discharge the red color of a solution containing 0.0987 Gm. $KMnO_4$. Such a quantity of crystallized oxalic acid is contained in 31.3 Cc. of a decinormal solution, for $0.196717 \div 0.006285 = 31.3$.

Since potassium permanganate is very easily decomposed, it should never be triturated or dispensed with readily oxidizable or organic substances. Stains produced by the salt in mortars or on the hands are best removed with oxalic acid solution, either alone or with a little sulphuric acid.

POTASSIUM SULPHATE. K_2SO_4. This salt, which, although rarely used in medicine or pharmacy, has been retained in the Pharmacopœia, is obtained partly as a bi-product in many chemical operations and partly from the mineral kainite, a natural potassium and magnesium sulphate.

For a long time potassium sulphate, on account of the hardness of its crystals, was preferred as a diluent in the preparation of Dover's powder, and is still to-day used by some for this purpose.

SOLUTION OF POTASSA. The official Liquor Potassæ can be made either by decomposition of a solution of pure potassium carbonate with milk of lime or by simple solution of 56 Gm. of potassa in 944 Gm. of distilled water. Both methods are recognized in the

Pharmacopœia, the latter being generally preferred by pharmacists, as a matter of convenience, while the former is followed by manufacturing chemists, for economical reasons. If simple solution of the potassa be employed, it is important that the percentage of KOH present be known, in order to insure a 5 per cent. solution; the above proportions are calculated for 90 per cent. potassa and the proper quantity of a higher or lower grade can be readily found by the directions given in the Pharmacopœia. Thus, if the potassa contains only 82 per cent. KOH, it will require 61 (5000÷82) Gm. of potassa and 939 Gm. of distilled water, for 61 Gm. at 82 per cent. are equal to 56 Gm. at 90 per cent., 50 Gm. being the result in both cases and yielding 1000 Gm. of a 5 per cent. solution.

The object, in the first process, of heating the bicarbonate in solution until effervescence ceases, is to convert it into monocarbonate, and thus obtain a purer article than if commercial potassium carbonate were used. By mixing the two liquids hot and boiling the mixture for ten minutes a more compact precipitate of calcium carbonate is produced, which settles rapidly and from which the solution of potassa can be more readily separated.

The process involves two simple reactions: 1. $2KHCO_3 = K_2CO_3 + CO_2 + H_2O$; 2. $K_2CO_3 + Ca(OH)_2 = 2KOH + CaCO_3$. Lime is used in excess of the theoretical requirement on account of its slight solubility, and experience has also taught that considerable dilution of the two liquids is necessary, as the reaction cannot be completed in concentrated solutions.

In order to preserve the quality of solution of potassa it is essential that it be kept in securely stoppered bottles, to avoid absorption of carbon dioxide; the bottles should be made of green glass, as flint ware is easily acted upon, and the stoppers should be thinly coated with paraffin or petrolatum, to prevent their becoming "fixed." Solution of potassa should never be filtered through paper, which is rapidly attacked by the alkali; large volumes are best decanted or siphoned from any sediment, while small quantities may be conveniently filtered through glass-wool or asbestos.

The official solution of potassa has a specific gravity of about 1.036 at 15° C. (59° F.), and should contain about 5 per cent. of potassium hydroxide, which is equal to about 27 grains in each fluidounce; its strength is determined volumetrically with normal acid, each Cc. of which corresponds to 0.05599 Gm. KOH.

Solution of Potassium Arsenite. This preparation can be more conveniently studied in connection with the preparations of arsenic.

Solution of Potassium Citrate. The Pharmacopœia very properly directs the extemporaneous preparation of this solution, as it does not keep well and soon loses its refreshing taste. The proportions of citric acid, 6 Gm., and potassium bicarbonate, 8 Gm., in the official formula show a slight excess of citric acid over the quan-

tity necessary to form a neutral salt, which improves the flavor of the finished product. The solution contains 8.16 Gm. of potassium citrate and 0.4 Gm. of citric acid in 100 Cc., besides some carbonic acid, which corresponds to about 38 grains of the salt in each fluid-ounce.

Although the Pharmacopœia has given the synonym, *mistura potassii citratis*, to this solution, it differs from the preparation formerly recognized by that name and more familiarly known as *neutral mixture*. The former preparation was made by neutralizing fresh lemon-juice, strained through cotton, with potassium bicarbonate, and possessed, therefore, a more agreeable flavor, although of uncertain strength. Some physicians still prefer the old *neutral mixture* to the present official solution in many cases.

Besides the potassium salts officially recognized, the following are occasionally used in medicine and pharmacy.

POTASSIUM BENZOATE. $KC_7H_5O_2+3H_2O$. This salt can be most conveniently obtained by adding benzoic acid to a solution of potassium bicarbonate and evaporating the resulting solution; 100 parts of benzoic acid require 82 parts of potassium bicarbonate for complete neutralization, yielding 175.5 parts of a salt having the above composition.

POTASSIUM CHLORIDE. KCl. This may be obtained as a by-product in the manufacture of other salts, but is chiefly derived from the mineral carnallite, a double potassium and magnesium chloride, extensively mined in Germany.

POTASSIUM SALICYLATE. $2KC_7H_5O_3+H_2O$. This can be readily prepared in the manner outlined for potassium benzoate, simply using salicylic acid in place of benzoic acid, 100 parts of the former requiring 72.5 parts of potassium bicarbonate and yielding 127.5 parts of the newly formed salt.

POTASSIUM SULPHITE. $K_2SO_3+2H_2O$. When sulphur dioxide is passed into a solution of potassium carbonate until the carbon dioxide has all been expelled and another portion of potassium carbonate equal in weight to that first used is then added, potassium sulphite will crystallize on concentration of the solution. If, in place of more potassium carbonate, strong alcohol be added to the solution carrying sulphur dioxide in excess, potassium bisulphite, $KHSO_3$, will crystallize out.

POTASSIUM TARTRATE. $K_2C_4H_4O_6+H_2O$. Normal potassium tartrate is made from the bitartrate by neutralizing the excess of acid present with potassium carbonate. The salt was dropped at the last revision of the U. S. Pharmacopœia, but is still recognized in the British and German Pharmacopœias.

CHAPTER XLI.

THE COMPOUNDS OF SODIUM.

THE official salts of sodium resemble those of potassium in many respects and are frequently prepared by analogous processes. Twenty-one salts, besides four liquid and three solid preparations, are recognized in the Pharmacopœia, as follows:

Official English Name.	Official Latin Name.
Soda,	Soda.
Sodium Acetate,	Sodii Acetas.
Sodium Arsenate,	Sodii Arsenas.
Sodium Benzoate,	Sodii Benzoas.
Sodium Bicarbonate,	Sodii Bicarbonas.
Sodium Bisulphite,	Sodii Bisulphis.
Sodium Borate,	Sodii Boras.
Sodium Bromide,	Sodii Bromidum.
Sodium Carbonate,	Sodii Carbonas.
Dried Sodium Carbonate,	Sodii Carbonas Exsiccatus.
Sodium Chlorate,	Sodii Chloras
Sodium Chloride,	Sodii Chloridum.
Sodium Hypophosphite,	Sodii Hypophosphis.
Sodium Hyposulphite (Thiosulphate),	Sodii Hyposulphis.
Sodium Iodide,	Sodii Iodidum.
Sodium Nitrate,	Sodii Nitras.
Sodium Nitrite,	Sodii Nitris.
Sodium Phosphate,	Sodii Phosphas.
Sodium Pyrophosphate.	Sodii Pyrophosphas.
Sodium Salicylate,	Sodii Salicylas.
Sodium Sulphate,	Sodii Sulphas.
Sodium Sulphite,	Sodii Sulphis
Sodium Sulphocarbolate,	Sodii Sulphocarbolas.
Solution of Soda,	Liquor Sodæ.
Solution of Chlorinated Soda,	Liquor Sodæ Chloratæ.
Solution of Sodium Arsenate,	Liquor Sodii Arsenatis.
Solution of Sodium Silicate,	Liquor Sodii Silicatis.
Troches of Sodium Bicarbonate,	Trochisci Sodii Bicarbonatis.

SODA. NaOH. The usual method of manufacture of sodium hydroxide, or caustic soda, is by decomposition of a solution of sodium carbonate by means of milk of lime, the filtrate, as in the case of potassa, being evaporated in silver or iron vessels, and finally allowed to congeal in suitable moulds. The product thus obtained is known as soda by lime. A purer article may be obtained either by direct action of metallic sodium on water or by purification of commercial soda with alcohol.

Like caustic potash, caustic soda is very deliquescent, and rapidly absorbs carbon dioxide upon exposure to the air; hence the same care

must be observed in its preservation in tightly stoppered green-glass bottles.

The Pharmacopœia makes similar requirements for soda as for potassa, in regard to the allowable limit of impurities, and also demands that official soda shall contain not less than 90 per cent. of absolute NaOH, which is volumetrically determined with normal acid, each Cc. of which is capable of neutralizing 0.03996 Gm. NaOH.

SODIUM ACETATE. $NaC_2H_3O_2 + 3H_2O$. This salt may be prepared by neutralizing acetic acid with sodium carbonate or bicarbonate, concentrating the resulting solution and crystallizing; in a crude form it is extensively obtained in the manufacture of acetic acid, and may be purified by roasting and other processes. Sodium acetate differs from potassium acetate in containing nearly 40 per cent. of water of crystallization, and in its stability upon exposure to air, hence less care is necessary in its preservation; it is about one-third as soluble in water and far less soluble in alcohol than the potassium salt.

The valuation of the so-called organic sodium salts is performed, as in the case of the corresponding potassium salts, by conversion into carbonate and subsequent titration with acid. The following equation, $2(NaC_2H_3O_2 + 3H_2O) + O_8 = Na_2CO_3 + 3CO_2 + 9H_2O$, shows that two molecules, or 271.48 parts, of crystallized sodium acetate yield, upon complete ignition, one molecule, or 105.85 parts, of anhydrous sodium carbonate; hence, each Cc. of $\frac{N}{1}$ H_2SO_4, neutralizing 0.052925 Gm. Na_2CO_3, corresponds to 0.13574 Gm. $NaC_2H_3O_2 + 3H_2O$. The Pharmacopœia demands that the official sodium acetate shall be 100 per cent. pure, and 1.36 Gm. of the salt must, therefore, after complete ignition, require 10 Cc. of normal acid to neutralize the alkaline residue, as stated in the official test.

SODIUM ARSENATE. $Na_2HAsO_4 + 7H_2O$. The official salt, as shown by the chemical formula, is disodium orthoarsenate, and bears a close analogy to the official sodium phosphate; the exact composition must depend upon the proportions of the ingredients used in its manufacture. Sodium arsenate is usually obtained by fusing together, at a red heat, arsenous oxide, dried sodium carbonate, and sodium nitrate; effervescence ensues, and, when complete quiet fusion has set in, the residue will consist of sodium pyroarsenate, as shown by the following equation: $As_2O_3 + 2NaNO_3 + Na_2CO_3 = Na_4As_2O_7 + N_2O_3 + CO_2$. The fused mass, having been poured on a stone slab and allowed to solidify, is dissolved, while still warm, in water, whereby the sodium pyroarsenate is converted into orthoarsenate by the appropriation of water, thus, $Na_4As_2O_7 + H_2O = 2Na_2HAsO_4$. The solution is set aside to crystallize, when a salt containing 40.4 per cent. of water, and having the above formula, will be obtained.

The British Pharmacopœia directs the following proportions:

Arsenous oxide 10 parts, sodium nitrate $8\frac{1}{2}$ parts, and dried sodium carbonate $5\frac{1}{2}$ parts; if an excess of sodium carbonate be used, trisodium arsenate, Na_3AsO_4, will be formed, while an excess of arsenic acid yields monosodium arsenate, NaH_2AsO_4.

The official salt, upon exposure to dry air, gradually loses a portion of its water of crystallization until a salt of the composition $Na_2HAsO_4 + 2H_2O$ remains, containing only 16.2 per cent. of water, hence, it should be preserved in tightly stoppered bottles.

Sodium Benzoate. $NaC_7H_5O_2$. This salt may be conveniently prepared by suspending benzoic acid in hot water and slowly adding sufficient sodium bicarbonate to form a neutral solution, which is then filtered and evaporated, with frequent stirring, on a water-bath, to dryness. 100 parts of benzoic acid require about 70 parts of official sodium bicarbonate and yield about 118 parts of sodium benzoate. The salt can also be obtained in crystalline form, having the composition $NaC_7H_5O_2 + H_2O$; but, as it effloresces readily, the Pharmacopœia has recognized only the anhydrous salt.

The valuation of sodium benzoate is made, like that of the acetate, by ignition and titration of the resulting sodium carbonate with normal acid. The equation, $2NaC_7H_5O_2 + O_{30} = Na_2CO_3 + 5H_2O + 13CO_2$, shows that 287.42 parts of sodium benzoate will yield 105.85 parts of anhydrous sodium carbonate, therefore each Cc. $\frac{N}{1}$ H_2SO_4 represents 0.14371 Gm. $NaC_7H_5O_2$. Using 2 Gm. of the salt, as directed in the official test, 13.9 Cc. $\frac{N}{1}$ H_2SO_4 will be required to neutralize the alkaline residue if 99.8 per cent. $NaC_7H_5O_2$ be present, for 99.8 per cent. of 2 is 1.996 and $0.1437 \times 13.9 = 1.997$.

Sodium Bicarbonate. $NaHCO_3$. This well-known compound is manufactured on a large scale by different processes. If sodium carbonate in crystalline form be treated with carbon dioxide, anhydrous sodium bicarbonate, or acid carbonate, will be formed and water eliminated; thus, $(Na_2CO_3 + 10H_2O) + CO_2 = 2NaHCO_3 + 9H_2O$; by using a mixture of anhydrous and crystallized sodium carbonate, a part of the eliminated water will be required for converting the former into bicarbonate, the balance being allowed to escape by drainage. Sodium bicarbonate is also obtained as an intermediate product in the manufacture of the normal carbonate by the Solvay ammonia-soda process, wherein concentrated solution of sodium chloride is mixed with ammonia and then saturated with carbon dioxide under pressure. Sodium bicarbonate is precipitated and ammonium chloride remains in solution. In either case the newly formed sodium bicarbonate is washed with small quantities of water for the purpose of removing the more soluble impurities.

The product of the Solvay process requires more careful purification, owing to contamination with ammonium salts, especially ammonium carbonate, hence sodium bicarbonate, prepared from normal carbonate, is preferred for medicinal purposes.

Commercial sodium bicarbonate is frequently contaminated with carbonate and chloride, but if a pure salt is wanted, this may be readily obtained by percolating the commercial article with cold distilled water and drying the purified residue with moderate heat only.

The Pharmacopœia does not require absolute purity for sodium bicarbonate, traces of carbonate, chloride, sulphate, and sulphite being permitted. The official salt must, however, contain at least 98.6 per cent. $NaHCO_3$, as indicated by the demand that 0.85 Gm. of the salt shall require not less than 10 Cc. $\frac{N}{1}$ H_2SO_4 for complete neutralization, each Cc. representing 0.08385 Gm. $NaHCO_3$.

Sodium Bisulphite. $NaHSO_3$. This salt, known also as acid sodium sulphite, is rarely used in medicine. It is prepared by passing sulphur dioxide into a solution of sodium carbonate to saturation and until all carbon dioxide has been expelled, the reaction being as follows: $Na_2CO_3+H_2O+2SO_2=2NaHSO_3+CO_2$. The solution is then concentrated and allowed to crystallize.

Sodium bisulphite is not a very stable compound, and upon exposure to air is gradually oxidized and converted into sulphate, sulphur dioxide being given off at the same time. Traces of sulphate and chloride are permitted in the official salt. The turbidity caused in a solution of the salt by addition of hydrochloric acid, indicating the presence of thiosulphate (hyposulphite), is due to finely precipitated sulphur.

The Pharmacopœia demands at least 90 per cent. of absolute $NaHSO_3$ in the official compound, which is determined volumetrically by means of iodine, the latter acting as an oxidizing agent, converting the acid sulphite into an acid sulphate; thus, $NaHSO_3+I_2+H_2O=NaHSO_4+2HI$. Since 103.86 parts of the acid sulphite require 253.06 parts of iodine for complete oxidation, each Cc. $\frac{N}{10}$ I solution containing 0.012653 Gm. of iodine is capable of oxidizing 0.005193 Gm. $NaHSO_3$ and 45 Cc. will be required to indicate 90 per cent. if 0.26 Gm. of the salt be used for the assay, as directed, for 90 per cent. of 0.26 is 0.234 and $0.005193\times45=0.2336+$. No permanent blue tint, due to formation of iodized starch, will occur until all sulphurous acid has been oxidized.

Sodium Borate. $Na_2B_4O_7+10H_2O$. The more familiar name borax is usually applied to this compound, which, although sometimes called sodium biborate, is, as shown by the chemical formula, sodium tetraborate or pyroborate. It is found extensively in different parts of the world, particularly in California, where immense quantities are obtained from the blue mud of certain lakes. Solution and recrystallization are resorted to for the purpose of purification. Considerable quantities of borax are also obtained from crude boric acid, by treating it with sodium carbonate, and from various minerals containing borates of sodium, calcium, and magnesium.

Borax is of special interest in pharmacy on account of its peculiar

behavior with other substances. It is incompatible with mucilage of acacia, causing gelatinization, which can, however, be prevented by the presence of sugar; it precipitates many alkaloids from their solution, such as cocaine, morphine, atropine, quinine, etc., except in the presence of glycerin; it forms a damp, almost moist, mixture when triturated with alum; in the presence of glycerin it decomposes alkali bicarbonates with effervescence; and, lastly, while an aqueous solution of borax shows an alkaline reaction toward litmus, a solution in glycerin has a decided acid reaction, which is changed to alkaline upon large dilution with water. This last behavior is also observed with other bodies resembling glycerin, such as mannitol, glucose, etc.

Sodium Bromide. NaBr. This salt is prepared in a manner similar to potassium bromide, either by decomposing a solution of ferrous bromide with sodium carbonate or by treating a solution of soda with bromine and finally reducing any sodium bromate formed with charcoal.

Sodium bromide is somewhat hygroscopic, but the Pharmacopœia has fixed the limit of moisture at 3 per cent. As in the case of the corresponding potassium salt, some chloride is usually present, which is volumetrically determined with decinormal silver nitrate solution, each Cc. of which is equivalent to 0.010276 Gm. NaBr or 0.005837 Gm. NaCl. The rule given under potassium bromide (page 434) may be used for finding the exact percentage of sodium chloride contained in any sample. The Pharmacopœia requires 97.29 per cent. of pure NaBr in the dry salt by demanding that not more than 29.8 Cc. $\frac{N}{10}$ $AgNO_3$ solution shall be necessary to precipitate completely 0.3 Gm. of the salt. This would indicate about 2.76 per cent. NaCl, for 0.3 Gm. of pure NaBr require 29.19 Cc. $\frac{N}{10}$ $AgNO_3$ solution, and each 0.221 Cc. used in excess of that quantity indicates 1 per cent. NaCl; then $29.8-29.19=0.61$ and $0.61\div0.221=2.76$.

Sodium Carbonate. $Na_2CO_3+10H_2O$. Three distinct processes are in use at the present day for the manufacture of this salt, namely, the Leblanc process of 1784, the cryolite process of 1851, and the Solvay ammonia process of 1873. In both the Leblanc and Solvay processes sodium chloride is employed as the starting-point. In the first case sodium chloride is converted into sodium sulphate by action of sulphuric acid, and then into sodium sulphide, and subsequently carbonate, by treatment with coal and chalk, calcium sulphide occurring as a waste product. In the ammonia process a solution of sodium chloride is treated with ammonia gas and carbon dioxide under pressure, when acid sodium carbonate and ammonium chloride are produced, together with some acid ammonium carbonate, which reacts with more sodium chloride, converting it into sodium bicarbonate. Finally the sodium bicarbonate is converted by heat into the normal carbonate.

The cryolite process consists in heating the powdered mineral

cryolite, a double sodium and aluminum fluoride ($AlF_3 3NaF$), with chalk or limestone, whereby a soluble sodium aluminate and insoluble calcium fluoride are produced, carbon dioxide being eliminated. By passing carbon dioxide under pressure into a solution of the sodium aluminate sodium carbonate is formed, as well as aluminum hydroxide, the latter being precipitated. This process is extensively employed in this country, large quantities of cryolite being brought from Greenland.

In each of the three processes the sodium carbonate formed is brought into solution, which is filtered, concentrated, and allowed to crystallize. The various steps in the manufacture of the salt can be conveniently shown by the following equations:

1. The Leblanc Process:
   a. $NaCl + H_2SO_4 = NaHSO_4 + HCl.$
   b. $NaHSO_4 + NaCl = Na_2SO_4 + HCl.$
   c. $Na_2SO_4 + C_4 = Na_2S + 4CO.$
   d. $Na_2S + CaCO_3 = Na_2CO_3 + CaS.$
2. The Solvay Process:
   a. $NaCl + 2NH_3 + 3CO_2 + 2H_2O = NaHCO_3 + NH_4HCO_3 + NH_4Cl.$
   b. $NaCl + NH_4HCO_3 = NaHCO_3 + NH_4Cl.$
   c. $2NaHCO_3 = Na_2CO_3 + CO_2 + H_2O.$
3. The Cryolite Process:
   a. $Na_3AlF_6 + 3CaCO_3 = Na_3AlO_3 + 3CaF_2 + 3CO_2.$
   b. $2Na_3AlO_3 + 3CO_2 + 3H_2O = 3Na_2CO_3 + 2Al(OH)_3.$

The official sodium carbonate contains 63 per cent. of water, but effloresces upon exposure to dry air, being gradually converted into a white powder. The crystallized salt is rarely used in medicine. The commercial salt is usually contaminated with chloride and sulphate, and is purified by recrystallization. The Pharmacopœia requires that the anhydrous salt, deprived of all water by heating immediately before being weighed, shall contain at least 98.9 per cent. of Na_2CO_3, as ascertained by titration with normal acid. The following equation, $Na_2CO_3 + H_2SO_4 = Na_2SO_4 + CO_2 + H_2O$, shows that each Cc. $\frac{N}{1}$ H_2SO_4 corresponds to 0.052925 Gm. absolute Na_2CO_3, hence 18.7 Cc. will represent 0.989 Gm. in the official test.

Dried Sodium Carbonate. This preparation is recognized in the Pharmacopœia partly with a view of supplying a more uniform product than the crystallized salt and partly for convenience in dispensing. By following the official directions a part of the water of crystallization is allowed to pass off at room temperature, by efflorescence, to avoid fusion of the salt at a higher temperature, after which the white powder is reduced to a definite weight by exposure to a moderate heat, the final residue still retaining about 26 per cent. of water, and probably corresponding in composition to the formula $Na_2CO_3 + 2H_2O$. In this condition sodium carbonate is somewhat hygroscopic and must be preserved in tightly stoppered bottles. The

official article should contain about 73 per cent. of absolute Na_2CO_3. The British Pharmacopœia requires an absolutely anhydrous salt.

SODIUM CHLORATE. $NaClO_3$. This salt may be prepared in a similar manner to potassium chlorate or by decomposing a solution of acid sodium tartrate or sodium silicofluoride with potassium chlorate ($NaHC_4H_4O_6 + KClO_3 = NaClO_3 + KHC_4H_4O_6$ or $Na_2SiF_6 + 2KClO_3 = 2NaCl + K_2SiF_6$), removing the precipitated potassium compound by filtration, concentrating the solution, and allowing the chlorate to crystallize.

Sodium chlorate is vastly more soluble in both water and alcohol than the corresponding potassium salt; but, like the latter, is readily decomposed when triturated with organic or other easily oxidizable substances, hence must be handled with care.

SODIUM CHLORIDE. NaCl. There is probably no substance so universally distributed over the world as common salt, nature providing it both in crystalline form, as rock-salt, or in solution, as sea-water and the brine of salt wells. Rock-salt is extensively mined, but the largest supply of salt is obtained by evaporation of the natural solutions.

Sodium chloride is employed in the manufacture of certain chemicals, but is used rarely in medicine, although an indispensable requisite in the animal system. It is of chief interest to pharmacists as a reagent in the volumetric valuation of silver salts.

SODIUM HYPOPHOSPHITE. $NaH_2PO_2 + H_2O$. Like the corresponding potassium salt, this salt may be conveniently made by decomposing a solution of calcium hypophosphite with sodium carbonate or sulphate. After removal of the calcium salt by filtration the solution is evaporated on a water-bath to dryness, with constant stirring for the purpose of granulation.

Sodium hypophosphite is hygroscopic, but more permanent than the potassium salt upon exposure to air, and explodes readily when triturated with nitrates, chlorates, or permanganates, owing to its tendency to oxidation.

The Pharmacopœia requires the official salt to contain not less than 97.96 per cent. of pure NaH_2PO_2, to be ascertained by titration with decinormal potassium permanganate solution. An excess of the reagent is added and the excess determined with oxalic acid solution, as explained under potassium hypophosphite. The equation $5(NaH_2PO_2 + H_2O) + 6H_2SO_4 + 4KMnO_4 = 5NaH_2PO_4 + 2K_2SO_4 + 4MnSO_4 + 11H_2O$ shows that 5 molecules or 529.2 parts of pure crystallized sodium hypophosphite require 4 molecules, or 630.68 parts, of potassium permanganate for complete oxidation; hence 1 Cc. $\frac{N}{10}$ $KMnO_4$ solution represents 0.002646 Gm. $NaH_2PO_2 + H_2O$.

SODIUM IODIDE. NaI. This salt may be prepared by adding iodine to a solution of caustic soda; but, since, on the reduction of

the resulting sodium iodate with charcoal, some sodium carbonate is apt to be formed, it is preferable to obtain the salt by double decomposition of ferrous or ferroso-ferric iodide with sodium carbonate. The reaction taking place in either case may be explained by the following equations: $FeI_2 + (Na_2CO_3 + 10H_2O) = 2NaI + FeCO_3 + 10H_2O$; $Fe_3I_8 + 4(Na_2CO_3 + 10H_2O) = 8NaI + 4CO_2 + Fe_3(OH)_8 + 36H_2O$. The mixture is boiled so as to facilitate separation of the iron compound by filtration, after which the filtrate is evaporated to dryness, with constant stirring, thus yielding a finely granulated salt.

Sodium iodide crystallizes, in an anhydrous state, at temperatures above 40° C. (104° F.), and this is the salt recognized by the Pharmacopœia; but at ordinary temperatures it takes up nearly 19.5 per cent. of water, and then has the composition $NaI + 2H_2O$; the latter salt is decidedly less hygroscopic than the official anhydrous salt, which readily absorbs moisture from the air. This fact explains the very marked development of heat when strong solutions of the anhydrous salt are made, due to a chemical union of the salt with water, whereas similar solutions of potassium iodide produce a decided reduction of temperature. The Pharmacopœia requires the absence of more than 5 per cent. of water, which may be due to the presence of hydrated crystals or may have been absorbed by the anhydrous salt.

Sodium iodide, as well as its aqueous solution, gradually undergoes decomposition upon exposure to light, becoming colored, hence both should be preserved in dark amber-colored bottles.

The official salt must contain not less than 98 per cent. of pure sodium iodide, as indicated by the demand that 0.5 Gm. of the well-dried salt shall require not less than 33.4 nor more than 34.5 Cc. $\frac{N}{10}$ $AgNO_3$ for complete precipitation. 0.5 Gm. of absolute NaI requires exactly 33.4 Cc., and any increase above this may be due to sodium bromide and chloride present, since both of these salts have a lower molecular weight than the iodide, and, consequently, require a greater relative amount of silver solution for precipitation.

Sodium Nitrate. $NaNO_3$. The immense nitre-beds of Chili and Peru furnish this salt in a more or less crude state; it is commercially known as Chili saltpetre, or cubic nitre, and is purified by repeated solution and crystallization.

Sodium nitrate is of comparatively little interest in pharmacy, but is extensively employed in the manufacture of nitric and sulphuric acids, potassium nitrate, etc. It differs from ordinary saltpetre in being hygroscopic and in its greater solubility in water and alcohol.

Sodium Nitrite. $NaNO_2$. This salt is interesting chiefly as the source of nitrous acid in the official process for the manufacture of ethyl nitrite in the preparation of spirit of nitrous ether. When sodium nitrate is heated with charcoal, starch, or similar reducing

agents, sodium nitrite is formed; but a better process consists in heating fused sodium nitrate for some time with lead in thin sheets, whereby the lead is gradually converted into lead oxide or litharge and the sodium salt is reduced to nitrite; thus, $2NaNO_3 + Pb_2 = 2NaNO_2 + 2PbO$. The fused mass is lixiviated with water, the solution treated with carbon dioxide to remove any lead possibly held in solution, filtered, and finally allowed to crystallize. By repeated recrystallization a very pure salt can be obtained containing 98 per cent. and over of absolute sodium nitrite.

On account of its deliquescent character and ready oxidation to nitrate upon exposure to air, the salt must be carefully preserved in tightly closed bottles.

The value of sodium nitrite depends upon the proportion of $NaNO_2$ present, which should be not less than 97.6 per cent., and is determined by measuring the volume of nitrogen dioxide (N_2O_2 or NO) obtainable from a given weight of the salt. Whenever sodium nitrite is brought together with potassium iodide and diluted sulphuric acid, nitrogen dioxide and iodine are liberated with the formation of sodium and potassium acid sulphates; by conducting the operation in special apparatus, permitting of the collection of the gas in a graduated tube, its volume can readily be measured, and from this the corresponding weight of sodium nitrite be calculated.

The equation, $NaNO_2 + KI + 2H_2SO_4 = NO + I + NaHSO_4 + KHSO_4 + H_2O$, shows that one molecule, or 68.93 Gm. of absolute $NaNO_2$ yields one molecule, or 29.97 Gm. of NO gas: but, since the gas is to be measured, it is necessary to ascertain the weight of a cubic centimeter of the same. It is well known that a liter of hydrogen weighs 0.0896 Gm.; hence a liter of any other gas must weigh as many times 0.0896 Gm. as the gas is heavier than hydrogen; nitrogen dioxide is 14.985 times as heavy as hydrogen, for equal volumes of the two gases weigh 2 and 29.97 respectively; a liter of NO gas must therefore weigh 14.985 times 0.0896 Gm. or 1.34256 Gm., which, divided by 1000, gives 0.00134256 Gm. as the weight of one cubic centimeter. But this weight is based on standard conditions—namely, a temperature of 0° C. (32° F.) and a barometric pressure of 760 Mm., and any change in these conditions must change the weight of a Cc. of gas. Gases are known to increase in volume to the extent of $\frac{1}{273}$ or 0.003663 for every 1° C., or 1.8° F., hence the weight of a Cc. of gas at any higher temperature can be ascertained by dividing the weight of it at 0° C. (32° F.) by the increased volume at the higher temperature; at 15° C. (59° F.), 1 Cc. of any gas at 0° C. has increasesd to $1 + (0.003663 \times 15)$ or 1.054945 Cc., and at 25 C. (77° F.) to $1 + (0.003663 \times 25)$ or 1.091575 Cc. One Cc. of NO gas, therefore, weighing 0.00134256 Gm. at 0° C. (32° F.) will weigh at 15° C. (59° F.) 0.0012726 Gm. ($0.00134256 \div 1.054945 = 0.0012726$), and at 25° C. (77° F.) 0.0012319 Gm. ($0.00134256 \div 1.091575 = 0.0012319$).

Since 29.97 Gm. of NO gas represent 68.93 Gm. of $NaNO_2$, as

shown by the above equation, each Cc. NO gas at 15° C. (59° F.), weighing 0.0012726 Gm., must represent 0.002926 Gm. $NaNO_2$; for 29.97 : 68.93 : : 0.0012726 : 0.002926 ; and each Cc. at 25° C. (77° F.), weighing 0.0012319 Gm., must represent 0.002833 Gm. $NaNO_2$; for 29.97 : 68.93 : : 0.0012319 : 0.002833. The Pharmacopœia requires that 0.15 Gm. of sodium nitrite shall yield, at 15° C. (59° F.), not less than 50 Cc. of NO gas, and, at 25° C. (77° F.), not less than 51.7 Cc., to show at least 97.5 per cent. pure $NaNO_2$; 97.6 per cent of 0.15 Gm. is 0.0146 +, and 0.002926×50, or $0.002833 \times 51.7 = 0.0146 +$. Slight solubility of the gas in the salt solution, and variations in barometric pressure, are overlooked in the official test, as they will not materially affect the result.

Sodium Phosphate. $Na_2HPO_4 + 12H_2O$. Phosphoric acid being tribasic, is capable of yielding three classes of alkali salts, known respectively as primary, secondary, and tertiary alkali phosphate. The official salt, as shown by the chemical formula, is the secondary, or dibasic sodium phosphate, which usually shows a neutral or only faintly alkaline reaction toward litmus, the primary phosphate having an acid and the tertiary phosphate a decidedly alkaline reaction. Disodium orthophosphate, as the official salt is also known, is made by decomposing a solution of acid calcium phosphate with sodium carbonate. The calcium salt is obtained by digesting calcined bone, or bone ash, with sulphuric acid, whereby the tricalcium phosphate (of which bone contains about 40 per cent.) is converted into acid calcium phosphate and calcium sulphate, the latter being precipitated; thus, $Ca_3(PO_4)_2 + 2H_2SO_4 = CaH_4(PO_4)_2 + 2CaSO_4$; the magma is then strained, and the resulting liquid, containing the acid calcium phosphate in solution, is mixed with sodium carbonate as long as precipitation occurs, whereby secondary sodium phosphate is produced, and remains in solution, while calcium carbonate is precipitated and carbon dioxide expelled; thus, $CaH_4(PO_4)_2 + 2Na_2CO_3 = 2Na_2HPO_4 + CaCO_3 + CO_2 + H_2O$. The mixture is filtered and the filtrate concentrated and allowed to crystallize.

The official sodium phosphate contains 60.3 per cent. of water of crystallization, a portion of which, about one-fourth, is lost by efflorescence upon exposure to air; moreover, carbon dioxide is gradually absorbed, the salt being converted into monosodium phosphate and acid sodium carbonate; hence it must be preserved in well-stoppered bottles, in a cool place. At the temperature of boiling water the salt can be made anhydrous; but, when exposed in this condition, it again absorbs water, gradually forming a salt of the composition, $Na_2HPO_4 + 7H_2O$, containing about 47 per cent. of water, which is permanent. Dried, granulated sodium phosphate occurs as an article of commerce, but should not be used when sodium phosphate is prescribed by physicians or in official formulas, as it contains, weight

for weight, about one and one-half times the amount of actual Na_2HPO_4.

The British Pharmacopœia directs the preparation of effervescent sodium phosphate, which contains about 20 per cent. of the anhydrous salt, together with sodium bicarbonate and tartaric and citric acids. Granulation is effected by placing the mixture in a dish heated to about 100° C. (212° F.), and stirring assiduously.

SODIUM PYROPHOSPHATE. $Na_4P_2O_7 + 10H_2O$. This salt is prepared by exposing crystallized sodium phosphate to gradually increased temperatures, when it first undergoes fusion at about 44° C. (111.2° F.); at 100° C. (212° F.) becomes anhydrous, and at a red heat, 300° C. (572° F.), is changed into a tetrabasic salt of pyrophosphoric acid by the further elimination of water. Two molecules of the crystallized phosphate yield one molecule of the pyrophosphate; thus, $2(Na_2HPO_4 + 12H_2O) = Na_4P_2O_7 + 25H_2O$. The dry residue is dissolved in water, and the solution set aside to crystallize.

The crystals of sodium pyrophosphate are difficult to reduce to fine powder, and are far less soluble in water than the orthophosphate.

SODIUM SALICYLATE. $NaC_7H_5O_3$. The official salt may be conveniently obtained by mixing sodium bicarbonate 10 parts and salicylic acid 16.5 parts with distilled water 10 parts, in a glass or porcelain vessel, and, when effervescence has ceased, evaporating the solution, at a temperature not exceeding 60° C. (140° F.), to dryness. It is essential that the solution be slightly acid, hence, if necessary, a trifling addition of salicylic acid may be made, since alkali salicylates, in the presence of an excess of alkali, absorb oxygen from the air and become colored. Sodium bicarbonate and pure monocarbonate are better suited than sodium hydroxide for neutralizing the acid, since strong bases are apt to form different salts with salicylic acid, such as $Na_2C_7H_4O_3$, although the acid is monobasic; these so-called secondary salicylates are less permanent and less soluble in water than the normal salts.

All contact with iron must be carefully avoided in the preparation of this salt, owing to the delicate reaction of salicylic acid with that metal, and filtration through ordinary filter-paper is apt to color a solution of the salicylate, hence, pure cotton or glass wool is preferable for straining.

SODIUM SULPHATE. $Na_2SO_4 + 10H_2O$. This salt is daily obtained as a by-product in numerous chemical processes, such as the manufacture of hydrochloric and nitric acids and magnesium carbonate, as well as the generation of carbon dioxide from sodium bicarbonate with sulphuric acid, in the manufacture of carbonated waters. It is purified, if necessary, by recrystallization.

The official salt, commonly known as Glauber's salt, contains 55.9 per cent. of water of crystallization and effloresces rapidly upon exposure to air.

For convenience in dispensing, the German Pharmacopœia directs the preparation of dried sodium sulphate, by exposing the crystallized salt to a moderate heat until its weight has been reduced to one-half, as in the case of dried sodium carbonate. The dehydrated salt is in the form of a white powder and represents double the weight of the crystallized salt.

Effervescent sodium sulphate is directed by the British Pharmacopœia to be made from the anhydrous salt, in the same manner as stated under sodium phosphate. It contains about 25 per cent. Na_2SO_4.

Sodium Sulphite. $Na_2SO_3 + 7H_2O$. Normal sodium sulphite is obtained by first preparing a solution of the acid sulphite, as already explained under sodium bisulphite, and then adding a weight of sodium carbonate equal to that first used, when a neutral salt will be formed; thus, $2NaHSo_3 + Na_2CO_3 = 2Na_2SO_3 + CO_2 + H_2O$. The solution is then evaporated and allowed to crystallize.

The official salt contains 50 per cent. of water of crystallization and is liable to be contaminated with the same impurities as the bisulphite; it effloresces upon exposure to air and, like the latter salt, is gradually converted into sulphate. The Pharmacopœia requires that the salt shall contain at least 96 per cent. of crystallized Na_2SO_3, which is determined by means of iodine solution, whereby all sulphite present is converted into sulphate. According to the equation, $Na_2So_3.7H_2O + I_2 = Na_2SO_4 + 2HI + 6H_2O$, each Cc. $\frac{N}{10}$I solution, containing 0.012653 Gm. of iodine, is capable of oxidizing 0.012579 Gm. of the crystallized sulphite, hence 48 Cc. will be required for 0.63 Gm. of the official salt.

Sodium Sulphocarbolate or Paraphenolsulphonate. $NaSO_3C_6H_4(OH) + 2H_2O$. When pure carbolic acid is mixed with an equal weight of sulphuric acid, a new compound is formed, to which the name sulpho-carbolic, or, more correctly, phenolsulphonic acid, has been given and which has the composition $HSO_3C_6H_4OH$; the acid is monobasic and is produced according to the equation, $C_6H_5(OH) + H_2SO_4 = HSO_3C_6H_4OH + H_2O$. Two varieties of this acid are known, the ortho- and paraphenolsulphonic acids, the formation of which depends upon the temperature at which the reaction is allowed to go on; in the cold, only the ortho variety is produced, while with moderate heat a mixture of the acids results, and at the temperature of boiling water only the para acid is obtained. Both varieties form clear solutions with water, but differ from each other in the character of their salts, both as regards solubility and form and constitution of the crystals.

The Pharmacopœia recognizes only the *para*-phenolsulphonate of

sodium, which is prepared by heating a mixture of equal weights of carbolic and sulphuric acids, on a boiling water-bath for six hours, diluting the new compound with water and neutralizing the hot liquid with an excess of barium carbonate. After filtration, the solution of barium sulphocarbolate is decomposed by means of sodium carbonate, filtered, concentrated, and set aside to crystallize. The decomposition involves a very simple reaction; thus, $Ba(SO_3C_6H_4(OH))_2 + Na_2CO_3 = 2NaSO_3C_6H_4(OH) + BaCO_3$. Lead carbonate may be used in place of the barium carbonate to neutralize the newly formed phenolsulphonic acid, as lead sulphocarbolate is also soluble in water.

The official salt contains about 15.5 per cent. of water of crystallization. The corresponding potassium sulphocarbolate is perfectly anhydrous, while the zinc salt crystallizes with 8 molecules or 25.94 per cent. of water.

SODIUM THIOSULPHATE. $Na_2S_2O_3 + 5H_2O$. This salt, wrongly called sodium hyposulphite, may be obtained in various ways, such as boiling a solution of sodium sulphite with sulphur ($Na_2SO_3 + S = Na_2S_2O_3$), adding iodine to a solution of sodium sulphite and sulphide ($Na_2SO_3 + Na_2S + I = Na_2S_2O_3 + 2NaI$), boiling sulphur with solution of soda ($6NaOH + S_{12} = Na_2S_2O_3 + 2Na_2S_5 + 3H_2O$), etc.; the process employed on a large scale, however, consists in decomposition of calcium thiosulphate in solution, by means of sodium carbonate or sulphate, insoluble calcium carbonate or sulphate being precipitated, while sodium thiosulphate remains in solution and is recovered, after filtration, by crystallization; the reaction may be thus indicated, $CaS_2O_3 + Na_2CO_3 = Na_2S_2O_3 + CaCO_3$. Calcium thiosulphate is obtained either from the residue left in the manufacture of sodium carbonate by the Leblanc process, known as alkali-waste, or from the gas-lime left in the purification of illuminating gas by dry lime. Both of these residues contain calcium sulphides which, upon exposure to the air, undergo oxidation and are converted into thiosulphate.

Unfortunately the Pharmacopœia has retained the old name, sodium hyposulphite, as the official title for this salt, which is not in conformity with the chemical formula indicating its composition. True sodium hyposulphite has the formula $NaHSO_2$, and may be prepared by treating a solution of sodium bisulphite with metallic zinc, whereby sodium hyposulphite and sulphite, together with zinc sulphite, are formed; thus, $3NaHSO_3 + Zn = NaHSO_2 + Na_2SO_3 + ZnSO_3 + H_2O$; this salt is used by dyers and calico-printers. Hyposulphites can be distinguished from thiosulphates by heating them, when the former break up into thiosulphates and water, while the latter yield sulphates and sulphides.

Sodium thiosulphate is employed to a limited extent in medicine, but its chief use in pharmacy is as a valuable chemical reagent in volumetric analysis. The official salt should contain at least 98.1

per cent. of pure crystallized $Na_2S_2O_3$, which is determined by means of decinormal iodine solution in the presence of starch. The reaction between iodine and sodium thiosulphate has already been explained in connection with the assay of chlorine water (page 409), and, since each Cc. of $\frac{N}{10}$ iodine solution requires 0.024764 Gm. $Na_2S_2O_35H_2O$, it follows that at least 9.9 Cc. must be added to a solution of 0.25 Gm. of the official salt before an excess will be indicated by the permanent blue color of iodized starch, for 98.1 per cent. of 0.25 is $0.02452 \times$ and $0.02476 \times 9.9 = 0.2451636$.

Solution of Soda. This preparation closely resembles the official solution of potassa, and can be made by either of the processes described on page 439, except that sodium salts are to be used in place of potassium salts. It has a spec. grav. of about 1.059 at 15° C. (59° F.).

Solution of soda should contain 5 per cent. by weight of absolute NaOH, equal to about 27 grains in each fluidounce, and, for reasons already stated in connection with solution of potassa, must be preserved in green-glass bottles with tightly fitting stoppers coated with paraffin.

The official solution of soda of the British Pharmacopœia is slightly weaker than our own (4.1 per cent.), while that of the German Pharmacopœia (liquor natrii caustici) contains 15 per cent., and that of the French Codex 23 per cent of caustic soda.

Solution of Chlorinated Soda. The Pharmacopœia directs that this solution shall be made by mixing strong solutions of 75 parts of chlorinated lime and 150 parts of sodium carbonate, whereby the lime salts are decomposed and precipitated as carbonate; since chlorinated lime consists of a mixture of calcium hypochlorite and chloride, the corresponding sodium salts will be present in the liquid after the above mixture has been filtered. The decomposition may be illustrated by the following equation: $Ca(ClO)_2 + CaCl_2 + 2Na_2CO_3 = 2NaClO + 2NaCl + 2CaCO_3$. The object of directing a hot solution of sodium carbonate to be used is to insure the formation of a dense precipitate of calcium carbonate, from which the liquid can be readily separated, otherwise much trouble will be experienced in filtration and washing.

The preparation is more familiarly known as Labarraque's solution, and owes its value as a disinfectant to the *available* chlorine present, by which is meant, not the total amount of chlorine in combination, but the amount present as hypochlorite, which can be eliminated as free chlorine by the aid of an acid; thus, $NaClO + HCl = NaCl + HClO$ and $HClO + HCl = Cl_2 + H_2O$. The solution should be preserved in dark bottles provided with rubber stoppers, as light is detrimental to its stability, and cork stoppers are gradually destroyed by the liquid. The escape of carbon dioxide upon the addition of hydrochloric acid to the solution, is due to the decomposition of

sodium carbonate, which is frequently present, owing to the variable composition of the chlorinated lime used in the manufacture.

The official solution must contain at least 2.6 per cent. by weight of available chlorine, which is determined by liberating the chlorine with hydrochloric acid and allowing the same to act upon potassium iodide; as explained under chlorine water (page 409), an equivalent quantity of iodine will be set free, the amount of which can be ascertained volumetrically with decinormal sodium thiosulphate solution, and from this the weight of chlorine liberated can be readily calculated. Each Cc. $\frac{N}{10}$ $Na_2S_2O_3+5H_2O$ solution, corresponding to 0.012653 Gm. of iodine, represents 0.003537 Gm. of chlorine, hence 50 Cc. will be required to decolorize the iodine liberated by 0.1742 Gm., 2.6 per cent. of 6.7 Gm. chlorine, in the official test.

A preparation very similar to the foregoing is the solution of chlorinated potassa, better known as Javelle water, or eau de Javelle; it is prepared by substituting an equivalent quantity of potassium carbonate for the sodium carbonate in the above process.

Solution of Sodium Arsenate. Like Fowler's solution, this preparation may be more conveniently considered with the official compounds of arsenic.

Solution of Sodium Silicate. This solution, under the name of liquid glass, or water-glass, is more extensively employed in the arts than by physicians. It is prepared by fusing together a mixture of finely powdered quartz and dried sodium carbonate, when sodium silicate is formed and carbon dioxide expelled; the resulting product is treated with boiling water, filtered, and the solution concentrated. The official solution has a specific gravity of 1.30 to 1.40, and contains about 33 per cent. by weight of a mixture of sodium trisilicate and tetrasilicate ($Na_2S_3O_7$ and $Na_2S_4O_9$), which salts are less alkaline than the metasilicate, Na_2SiO_3, and, therefore, better adapted for surgical purposes.

Besides the official salts of sodium, the following are of interest to pharmacists:

Sodium Citrate. $2Na_3C_6H_5O_7+11H_2O$. Citric acid, being tribasic, is capable of forming three different salts with sodium, but the normal salt, or trisodium citrate, is the kind usually employed. It is prepared by neutralizing a solution of citric acid with sodium carbonate or bicarbonate, concentrating the solution and allowing it to crystallize. To make 100 parts of the salt requires 58.8 parts of citric acid and 121.5 parts of crystallized sodium carbonate or 71.6 parts of bicarbonate. The German Pharmacopœia recognizes, under the name Potio Riveri, a freshly prepared effervescent solution of sodium citrate, made with 4 Gm. of citric acid, 7 Gms. of crystallized sodium carbonate, and 190 Cc. of water.

SODIUM ETHYLATE. C_2H_5ONa. This salt, also known as caustic alcohol, is obtained by direct action of metallic sodium on absolute alcohol, the metal being added in small pieces at a time, as long as the evolution of hydrogen continues, and the mixture kept cool by immersing the flask in water. The salt may be preserved in the form of crystals or powder in well-stoppered bottles. The British Pharmacopœia directs a solution of sodium ethylate, to be made by dissolving 22 grains of metallic sodium in 1 fluidounce of absolute alcohol; it is a colorless, syrupy liquid, containing 19 per cent. of the salt, and becoming brown by keeping.

SODIUM SANTONINATE. $2NaC_{15}H_{19}O_4+7H_2O$. This salt, which was dropped from the Pharmacopœia of 1890, can be made by dissolving santonin in a hot solution of soda, filtering the solution and crystallizing in a cool place. It is soluble in 3 parts of water and 12 parts of alcohol at ordinary temperature.

SODIUM SULPHOVINATE, OR ETHYLSULPHATE. $NaC_2H_5SO_4+H_2O$. When sulphuric acid is added gradually to an equal weight of alcohol, sulphovinic or ethylsulphuric acid is formed; thus, $C_2H_5OH+H_2SO_4=C_2H_5HSO_4+H_2O$; this can be neutralized by adding barium carbonate in excess, filtering the mixture and decomposing the solution of barium sulphovinate by a solution of sodium carbonate or sulphate. After filtration the clear liquid is evaporated at a moderate heat and crystallized. The salt is very soluble in water and also in alcohol and glycerin.

SODIUM TARTRATE. $Na_2C_4H_4O_6+2H_2O$. This salt may be prepared, like the citrate, by simple substitution of tartaric acid for citric acid. To make 100 parts requires 65.19 parts of tartaric acid and 125.73 parts of crystallized sodium carbonate, or 74.09 parts of bicarbonate.

SODIUM VALERIANATE. $NaC_5H_9O_2$. This salt is recognized in the British Pharmacopœia, and is made by neutralizing valerianic acid with caustic soda or sodium carbonate; the solution is evaporated to dryness and the heat then continued until the salt fuses. If the valerianic acid is contaminated with amyl valerianate (apple oil), this will separate, and, floating as an oily liquor on the solution, can be removed.

CHAPTER XLII.

THE COMPOUNDS OF LITHIUM.

FIVE lithium salts are recognized in the Pharmacopœia together with one effervescent preparation of a salt. A peculiarity of all lithium salts, by which they can be readily distinguished from other alkali salts, is their complete solubility in a mixture of equal volumes of alcohol and ether, after conversion into the chloride.

The following is a list of the official lithium preparations:

Official English Name.	Official Latin Name.
Lithium Benzoate,	Lithii Benzoas.
Lithium Bromide,	Lithii Bromidum.
Lithium Carbonate,	Lithii Carbonas.
Lithium Citrate,	Lithii Citras.
Effervescent Lithium Citrate,	Lithii Citras Effervescens.

LITHIUM BENZOATE. $LiC_7H_5O_2$. This salt is most conveniently prepared from the carbonate, by suspending the same in hot water and adding benzoic acid as long as effervescence continues; the filtrate is evaporated on a water-bath to dryness, with constant stirring, or may be concentrated and set aside to crystallize. To make 100 parts of the salt will require 29 parts of lithium carbonate and 95 parts of benzoic acid, the reaction being as follows: $2HC_7H_5O_2 + Li_2CO_3 = 2LiC_7H_5O_2 + CO_2 + H_2O$.

The salt is permanent in the air and very soluble in water, but less so in alcohol. The Pharmacopœia requires practically absolute purity, which is determined as in the case of organic salts of the other alkalies. Two molecules, or 255.44 parts, of lithium benzoate yield, upon thorough ignition, 1 molecule, or 73.87 parts, of lithium carbonate; hence each Cc. $\frac{N}{1}$ H_2SO_4, capable of neutralizing 0.036935 Gm. of Li_2CO_3, must correspond to 0.12772 Gm. $LiC_7H_5O_2$. 1 Gm. of lithium benzoate, after ignition, will therefore require 7.8 Cc. $\frac{N}{1}$ H_2SO_4 to indicate 99.6 per cent. of the pure salt; for $0.12772 \times 7.8 = 0.996116$.

LITHIUM BROMIDE. LiBr. For the preparation of this salt diluted hydrobromic acid may be neutralized with lithium carbonate, or the latter salt may be agitated in a flask with a hot solution of ferrous bromide. The first method is probably the most desirable. Owing to the very deliquescent character of the salt it is not readily crystallized, and is preferably obtained in granular powder form by evaporating the solution to dryness on a water-bath.

Lithium bromide contains about 92 per cent. of bromine, a larger proportion than any other salt. It is very soluble in water and

alcohol, and also soluble in ether, and must be carefully preserved in well-stoppered bottles.

The salt is likely to be contaminated with lithium chloride (due to chlorine in the bromine), and the Pharmacopœia permits an admixture of 2 per cent. of this impurity, as shown by the official volumetric test. 0.3 Gm. of absolutely pure lithium bromide require only 34.57 Cc. $\frac{N}{10}$ $AgNO_3$ solution for complete precipitation, and 0.3 Gm. pure lithium chloride require 70.79 Cc.; according to the rule on page 434, each 0.3622 Cc. of the silver solution used in excess of 34.57 Cc. in the official test indicates 1 per cent. of LiCl and 0.73 Cc. (35.3-34.57=0.73) divided by 0.3622 is equal to 2.

LITHIUM CARBONATE. Li_2CO_3. The carbonate, the parent salt of the other lithium compounds, is obtained from the mineral lepidolite, a mixture of silicates and fluorides of potassium, sodium, aluminum, and lithium. By digestion with sulphuric acid impure lithium sulphate is obtained, which is freed from the other salts by crystallization, treatment with milk of lime, etc. The final solution of alkali hydroxides is mixed with ammonium carbonate, whereby the lithium carbonate is precipitated; or the mixed alkali hydroxides may be converted into chlorides, and the solution then treated with ammonium carbonate. For the purpose of purification lithium carbonate may be suspended in water and treated with carbon dioxide, when an acid carbonate, $LiHCO_3$, will be formed and enter into solution, upon heating which pure lithium carbonate will be precipitated.

Lithium carbonate is the least soluble of all alkali carbonates, and is, moreover, only a little more than half as soluble in boiling water as in cold water. It occurs in commerce as a light, odorless powder.

The Pharmacopœia requires that 0.5 Gm. of the salt suspended in water shall neutralize not less than 13 4 Cc. of normal acid, indicating at least 98.98 per cent. of pure Li_2CO_3; since each Cc. $\frac{N}{1}$ H_2SO_4 requires 0.036935 Gm. of the pure carbonate; 0.5 Gm. of the official salt must neutralize at least 13.4 Cc.; for 98.98 per cent. of 0.5 is 0.4949 and $13.4 \times 0.036935 = 0.4949$.

LITHIUM CITRATE. $Li_3C_6H_5O_7$. This salt can be prepared by adding lithium carbonate to a solution of citric acid until the latter is neutralized and evaporating the liquid to dryness, gradually raising the temperature to 115° C. (239° F.). As shown by the equation, $2H_3C_6H_5O_7.H_2O + 3Li_2CO_3 = 2Li_3C_6H_5O_7 + 3CO_2 + 5H_2O$, 419 parts of citric acid require 221.61 parts of lithium carbonate, the yield of citrate being equal to the weight of acid used.

As shown by the chemical formula given for the official salt, the Pharmacopœia recognizes only the anhydrous salt. If the abovementioned solution be concentrated and allowed to crystallize, the resulting salt will have the formula $Li_3C_6H_5O_7 + 4H_2O$, and contain 25.5 per cent. of water of crystallization, one-fourth of which cannot

be eliminated at a temperature of a boiling water-bath; this is the salt recognized in the British Pharmacopœia.

Both the anhydrous salt in powder form and the crystallized salt occur in commerce.

Since 3 molecules of lithium carbonate invariably yield 2 molecules of the normal citrate, so inversely 2 molecules, or 419.14 parts, of lithium citrate will, upon ignition, yield 3 molecules, or 221.61 parts, of the carbonate. In the official method of valuation of lithium citrate the alkaline residue left after ignition of 1 Gm. of the salt is required to neutralize at least 14.2 Cc. of normal acid, showing not less than 99.2 per cent. of anhydrous citrate. Each Cc. $\frac{n}{1}$ H_2SO_4 requiring 0.036935 Gm. Li_2CO_3 for saturation corresponds to 0.0698566 Gm. $Li_3C_6H_5O_7$ and $14.2 \times 0.0698566 = 0.99196$, which is equal to 99.2 per cent. of 1 Gm.

Effervescent Lithium Citrate. This preparation does not contain lithium citrate in the finished product, but the salt is intended to be formed when the official powder is dissolved in water; it is simply a mechanical mixture of the ingredients ordered by the Pharmacopœia. The amount of citric acid ordered in the official formula is sufficient to decompose both the lithium and sodium carbonates, leaving at the same time a slight excess of free acid, which amounts to about 7.7 Gm. in the total finished product. Each Gm. of the effervescent powder will yield, upon solution, 0.132 Gm. of anhydrous lithium citrate.

The amount of sugar required in the preparation will depend, in part, upon the loss of weight in drying the citric acid as directed by the Pharmacopœia.

The powder must be preserved in a dry, cool place.

Lithium Salicylate. $LiC_7H_5O_3$. This salt may be prepared by heating a mixture of 44 parts of salicylic acid, 12 parts of lithium carbonate, and 100 parts of water until effervescence ceases; it is then filtered and the solution evaporated to dryness. As in the case of sodium salicylate, a slight excess of acid is necessary to avoid discoloration of the finished product, and contact with metal must be carefully avoided.

Upon ignition, 2 molecules, or 287.36 parts, of lithium salicylate yield 1 molecule, or 73.87 parts, of the carbonate, and each Cc. of normal acid neutralized by the alkaline residue corresponds to 0.14368 Gm. $LiC_7H_5O_3$; 13.8 Cc. $\frac{n}{1}$ H_2SO will therefore be required to indicate 99.13 per cent. if 2 Gm. of the salt be used, as directed in the official volumetric test.

CHAPTER XLIII.

THE COMPOUNDS OF AMMONIUM.

ALTHOUGH, thus far, all efforts to isolate the basylous radical of ammonium salts have failed, the existence of the hypothetical body NH_4 must be assumed, as, without it, it would be impossible to explain the formation and composition of a large and important class of compounds in accordance with accepted modern views regarding the replacement of hydrogen in acids. The decomposition of sodium amalgam by means of ammonium chloride, resulting in the production of sodium chloride and a new spongy amalgam having a metallic lustre, points strongly to the metallic character of the radical called ammonium. The indirect source of all ammonium salts is the gaseous body ammonia, NH_3, which may be looked upon as ammonium hydroxide minus water, $NH_4OH - H_2O = NH_3$; a characteristic feature of these salts is their complete volatilization upon application of heat.

The Pharmacopœia recognizes 7 salts of ammonium, 4 preparations of the salts, and 3 solutions of the hydroxide, as follows:

Official English Name.	Official Latin Name.
Ammonium Benzoate.	Ammonii Benzoas.
Ammonium Bromide,	Ammonii Bromidum.
Ammonium Carbonate,	Ammonii Carbonas.
Ammonium Chloride,	Ammonii Chloridum.
Ammonium Iodide,	Ammonii Iodidum.
Ammonium Nitrate,	Ammonii Nitras.
Ammonium Valerianate,	Ammonii Valerianas.
Ammonia Water,	Aqua Ammoniæ.
Stronger Ammonia Water,	Aqua Ammoniæ Fortior.
Liniment of Ammonia,	Linimentum Ammoniæ.
Solution of Ammonium Acetate,	Liquor Ammonii Acetatis.
Spirit of Ammonia,	Spiritus Ammoniæ.
Aromatic Spirit of Ammonia,	Spiritus Ammoniæ Aromaticus.
Troches of Ammonium Chloride,	Trochisci Ammonii Chloridi.

AMMONIUM BENZOATE. $NH_4C_7H_5O_2$. When benzoic acid is added to diluted ammonia water, the acid is neutralized and ammonium benzoate is formed, which, remaining in solution, may be obtained in colorless crystals, if the liquid be concentrated by aid of a moderate heat and set aside. As ammonium salts are readily decomposed by heat, the liquid should be kept alkaline by the occasional addition of ammonia water during evaporation. To prepare 100 Gm. of the salt requires 87.75 Gm. of benzoic acid and 123 Gm. of official ammonia water.

AMMONIUM BROMIDE. NH_4Br. Decidedly the best method of preparing this salt is by double decomposition between boiling hot

concentrated solutions of ammonium sulphate and potassium bromide, when, upon cooling, the newly formed potassium sulphate is precipitated, while ammonium bromide remains in solution. To facilitate the removal of the potassium sulphate, alcohol is usually added to the cool liquid. The salt may be obtained in granular form by decanting the solution, concentrating it, and evaporating to dryness, with constant stirring.

Ammonium bromide may also be obtained quite pure by heating in a retort, on a sand-bath, an intimate mixture of potassium bromide and dried ammonium sulphate, and subliming the vapors of ammonium bromide in a suitable condenser.

The Pharmacopœia demands that not more than 1 per cent. of ammonium chloride shall be present in the official salt, by directing that 0.3 Gm. of it shall require not more than 30.9 Cc. of decinormal silver solution for precipitation. Since 0.3 Gm. of pure NH_4Br require 30.7 Cc. $\frac{N}{10}$ $AgNO_3$ solution and 0.3 Gm. of pure NH_4Cl require 56.2 Cc., the use of 30.9 Cc. really indicates a trifle less than 1 per cent. of chloride (about 0.78 per cent.); but, for all practical purposes, it may be assumed to be 1 per cent.

Ammonium Carbonate. $NH_4HCO_3NH_4NH_2CO_2$. As shown by the chemical formula, the official salt is not the normal carbonate, which would have the composition $(NH_4)_2CO_3$, but is a mixture of acid ammonium carbonate and ammonium carbamate. It is obtained on an extensive scale by heating ammonium chloride with an excess of chalk and condensing the resulting vapors in leaden chambers; it is afterward resublimed. The decomposition is accompanied by the splitting off of ammonia and water; hence the composition of the sublimate, as given in the Pharmacopœia: $4NH_4Cl + 2CaCO_3 = NH_4HCO_3NH_4NH_2CO_2 + 2CaCl_2 + NH_3 + H_2O$.

The commercial ammonium carbonate is usually accompanied by empyreuma, to which its peculiar tarry odor is due, and for pharmaceutical purposes only the purified article should be employed. Owing to the rapid deterioration of the salt under exposure to air, by the loss of both ammonia and carbon dioxide, it should be preserved in tightly closed bottles, the best container being a wide-mouth fruit jar provided with a rubber ring and metal clasp for hermetically sealing the glass top. Only firm translucent pieces of ammonium carbonate should be used, as the opaque friable condition is indicative of chemical change causing the conversion of the salt into acid- or bicarbonate.

When the official ammonium carbonate is dissolved in water it is converted into the so-called sesquicarbonate, a mixture of acid and normal carbonate; thus, $NH_4HCO_3NH_4NH_2CO_2 + H_2O = NH_4HCO_3 (NH_4)_2CO_3$. The Pharmacopœia requires that the official salt shall be absolutely pure, and, in the volumetric valuation with normal acid, 2.613 Gm. are required to neutralize 50 Cc. $\frac{N}{1}H_2SO_4$. The test can be explained as follows: Upon solution in water, as pre-

viously stated, 156.77 parts of the official carbonate are changed to 174.73 parts of the mixed acid and normal carbonates, which are decomposed by the sulphuric acid, forming ammonium sulphate with elimination of carbon dioxide and water, as shown by the following equation: $2(NH_4HCO_3 + (NH_4)_2CO_3) + 3H_2SO_4 = 3(NH_4)_2SO_4 + 4CO_2 + 4H_2O$. Since 349.46 parts of the mixed carbonates, representing 313.54 parts of the official carbonate, can neutralize 293.46 parts of absolute sulphuric acid, each Cc. $\frac{N}{1}H_2SO_4$ containing 0.04891 Gm. H_2SO_4, must correspond to 0.05226 Gm. of the official carbonate (for 293.46 : 313.54 : : 0.04891 : 0.05226) and 2.613 Gm. of the official salt must neutralize 50 Cc. of normal acid, because $2.613 \div 0.05226$ is equal to 50.

Ammonium Chloride. NH_4Cl. Crude ammonium chloride is obtained by neutralizing the ammoniacal gas-liquors, condensed in the preparation and purification of illuminating gas from coal, with hydrochloric acid, evaporating the solution to dryness and subliming the salt in iron vessels. This product, being usually contaminated with iron, is, for pharmaceutical purposes, purified by adding ammonia water to a hot solution of the salt, filtering to remove the precipitated ferric hydroxide, and evaporating the filtrate, with constant stirring so as to form a granular powder.

Ammonium Iodide. NH_4I. This salt is most conveniently prepared by double decomposition between potassium iodide and ammonium sulphate dissolved in a small quantity of boiling water; when the mixture has cooled, alcohol is added to insure a more perfect separation of the newly formed potassium sulphate, and the solution of ammonium iodide is filtered and evaporated to dryness, constantly stirring. The reaction is as follows: $2KI + (NH_4)_2SO_4 = 2NH_4I + K_2SO_4$.

Ammonium iodide must be preserved in tightly stoppered dark bottles, as it is very hygroscopic and is readily decomposed when exposed to air and light. As the Pharmacopœia directs, the salt should never be dispensed after it has become deeply colored, but may be restored to its original condition by dissolving in as little water as possible, adding solution of ammonium sulphide until the color is discharged, then filtering to remove the precipitated sulphur and evaporating on a water-bath to dryness. The ammonium sulphide added undergoes decomposition, uniting with the free iodine to form ammonium iodide, while sulphur is precipitated at the same time; thus, $(NH_4)_2S + I_2 = 2NH_4I + S$.

The official test for the presence of ammonium bromide and chloride depends upon the very sparing solubility of silver iodide in water; hence any turbidity or precipitate produced in the ammoniacal filtrate upon the addition of nitric acid must be due to the presence of silver bromide or chloride. If the ammonium iodide be absolutely pure, 17.3 Cc. $\frac{N}{10}$ $AgNO_3$ solution will suffice for complete precipi-

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[illegible] NH[illegible]N[illegible] [illegible]

[illegible] NH[illegible]N[illegible]=N[illegible]

[illegible] NH[illegible]H[illegible]

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gas into water; when made by this process the solution generally is less pure, being accompanied by empyreuma.

Ammonia gas is very soluble in water, which, at 0° C. (32° F.), is capable of taking up 1050 volumes of the gas, and even at 15° C. (59° F.) retains 727 volumes in solution. The official ammonia water contains about 125 volumes of gas; that is, 1 Cc. holds 125 Cc. of ammonia gas in solution.

Different grades of strength of ammonia water are found in commerce, of which that designated as 16° corresponds to the official 10 per cent. solution; but it must be borne in mind that ammonia water is apt to deteriorate, by loss of ammonia gas, when kept in loosely stoppered vessels, such as carboys, especially if stored in a warm place. Ammonia water should be preserved in glass-stoppered bottles, although sound corks may be used if not allowed to come in contact with the liquid, by covering with prepared bladder, as small particles of cork allowed to fall into the liquid soon impart a yellowish color to the same.

Ammonia water is commonly known as *spirit of hartshorn;* in the British Pharmacopœia it is recognized as *solution of ammonia*, and in the German Pharmacopœia as *solution of caustic ammonia.*

The strength of ammonia water is determined by titration with normal acid, each Cc. of which requires 0.01701 Gm. NH_3 for neutralization; hence, if 3.4 Gm. of the water be used for the test, as officially directed, 20 Cc. $\frac{N}{5}H_2SO_4$ should be necessary to produce a neutral solution, indicating the presence of 10 per cent. of ammonia gas; for 10 per cent. of 3.4 is 0.34, and $0.01701 \times 20 = 0.342$.

Stronger Ammonia Water. This preparation differs from the preceding only in strength, containing 28 per cent. by weight of ammonia gas, and is prepared in a similar manner, except that the gas must be conducted into the cold water for a longer period of time, so that a greater amount may be absorbed.

Stronger ammonia water is not used in medicine, but has been found a very convenient source of supply for small quantities of pure ammonia gas, by simply heating in a flask provided with a delivery-tube, and for this purpose has been officially recognized. It can also be employed for the manufacture of weaker solutions of ammonia, which can be prepared of any desired strength by diluting the stronger ammonia water with plain water in proper proportions by weight, as explained on page 66. On account of the readiness with which all solutions of ammonia part with the gas upon an elevation of temperature, care should be exercised in opening bottles containing stronger water of ammonia, as serious accidents have been known to occur from the sudden expulsion of the liquid upon loosening the stopper, due to an accumulation of gas in the vessel.

The commercial grade known as 26° ammonia water corresponds to the official stronger solution. It should be purchased only in glass-stoppered bottles and preserved in a cool place.

to the official formula, by dissolving 5 Gm. of ammonium carbonate (in firm pieces) in 100 Cc. of diluted acetic acid, the finished product will contain 0.073 + Gm. of ammonium acetate in each Cc. (about 33 grains in each fluidounce), together with a trifling amount of acetic acid; to the latter, as well as to the carbon dioxide remaining in solution, the pleasant, refreshing taste of the preparation is due. 100 Cc. of diluted acetic acid contain 6.048 Gm. of absolute acetic acid, of which, according to the equation, $NH_4HCO_3NH_4NH_2CO_2 + 3HC_2H_3O_2 = 3NH_4C_2H_3O_2 + H_2O + 2CO_2$, 5.7274 Gm. are required to saturate 5 Gm. of ammonium carbonate.

The following unofficial salts of ammonium are sometimes used:

Ammonium Bicarbonate. NH_4HCO_3. This salt has already been mentioned, in connection with the official carbonate, as the white pulverulent decomposition-product obtained when the official salt is exposed to air. It may be prepared either by treating official ammonium carbonate with twice its weight of water, when the carbamate will be dissolved, leaving the acid- or bi-carbonate; or the official salt may be kept for two weeks under a bell-glass over sulphuric acid and lime, when the carbamate will be decomposed into carbon dioxide and ammonia, which are absorbed by the acid and lime, leaving the bicarbonate as a friable mass. When perfectly dry, ammonium bicarbonate is free from ammoniacal odor; it is soluble in 8 parts of water at 15° C. (59° F.), but is insoluble in alcohol.

Ammonium Citrate. $(NH_4)_3C_6H_5O_7$. This may be prepared by neutralizing a solution of citric acid with ammonium carbonate or ammonia water and carefully evaporating the solution on a water-bath, adding a little ammonia water from time to time, as the salt is readily decomposed. 100 Gm. of citric acid require for neutralization either 74.83 Gm. of ammonium carbonate or 243.58 Gm. of ten per cent. ammonia water, yielding 124.36 Gm. of a salt of the above composition.

Ammonium Phosphate. $(NH_4)_2HPO_4$. The British Pharmacopœia directs this salt to be prepared by adding stronger ammonia water to diluted phosphoric acid until a slight alkaline reaction ensues, then evaporating the solution with occasional addition of ammonia water and setting the liquid aside so that crystals may form, which must be quickly dried on paper.

Ammonium Salicylate. $NH_4C_7H_5O_3$. This may be prepared, like the corresponding potassium salt, by neutralizing salicylic acid with the alkali carbonate and carefully evaporating the solution to dryness. 100 parts of salicylic acid require 37.96 parts of the

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CHAPTER XLIV.

THE COMPOUNDS OF BARIUM, CALCIUM, AND STRONTIUM.

THE compounds of these three metals used in pharmacy are comparatively few in number, and may be conveniently grouped together. While there is but one official compound of barium, the Pharmacopœia recognizes ten compounds of calcium and seven preparations of the same, but only three compounds of strontium. The following list embraces all that are officially recognized:

Official English Name.	Official Latin Name.
Barium Dioxide,	Barii Dioxidum.
Calcium Bromide,	Calcii Bromidum.
Precipitated Calcium Carbonate,	Calcii Carbonas Præcipitatus.
Prepared Chalk,	Creta Præparata.
Calcium Chloride,	Calcii Chloridum.
Calcium Hypophosphite,	Calcii Hypophosphis.
Precipitated Calcium Phosphate,	Calcii Phosphas Præcipitatus.
Dried Calcium Sulphate,	Calcii Sulphas Exsiccatus.
Lime,	Calx.
Lime Liniment,	Linimentum Calcis.
Chlorinated Lime,	Calx Chlorata.
Sulphurated Lime,	Calx Sulphurata.
Solution of Lime,	Liquor Calcis.
Syrup of Lime,	Syrupus Calcis
Syrup of Calcium Lactophosphate,	Syrupus Calcii Lactophosphatis.
Chalk Mixture,	Mistura Cretæ.
Compound Chalk Powder,	Pulvis Cretæ Compositus.
Troches of Chalk,	Trochisci Cretæ.
Strontium Bromide	Strontii Bromidum.
Strontium Iodide,	Strontii Iodidum.
Strontium Lactate.	Strontii Lactas.

The Compounds of Barium.

BARIUM DIOXIDE. BaO_2. This compound is of interest because it is used in the preparation of solution of hydrogen dioxide intended for medicinal use. It is obtained by passing a current of air over barium oxide heated to about 450° C. (842° F.), when another atom of oxygen is taken up and the dioxide produced. The anhydrous commercial dioxide is recognized in the Pharmacopœia, which must contain, however, not less than 80 per cent. of pure BaO_2. The valuation is made by determining, with potassium permanganate, the quantity of hydrogen dioxide produced from a given weight of barium dioxide. The equation, $BaO_2 + H_3PO_4 = BaHPO_4 + H_2O_2$, shows that one molecule, or 168.82 parts, of barium dioxide, when

treated with phosphoric acid, yields one molecule, or 33.92 parts, of hydrogen dioxide, and since 1 Cc. $\frac{1}{10}$ $KMnO_4$ solution requires, for complete decoloration, 0.001696 Gm. H_2O_2, as shown on page 407, it follows that each Cc. so decolorized will correspond to 0.008441 Gm. BaO_2: for 33.92 : 169.62 :: 0.001696 : 0.008441.

In the official test, 2.11 Gm. barium dioxide are dissolved, with the aid of 7.5 Cc. of phosphoric acid, in sufficient ice-cold water to make 25 Cc. of solution, and to 5 Cc. of this solution, representing 0.422 Gm. BaO_2, decinormal potassium permanganate solution is added from a burette until a permanent pink tint is produced. As each Cc. $\frac{1}{10}$ $KMnO_4$ solution represents 0.008441 Gm. BaO_2, 40 Cc. will be necessary to show 80 per cent. of pure BaO_2 in 0.422 Gm.; for 80 per cent. of 0.422 is 0.3376 and 0.008441 × 40 = 0.33764.

Barium dioxide must be preserved in tightly closed vessels to prevent the absorption of moisture and carbon dioxide from the air.

The Compounds of Calcium.

Calcium Bromide. $CaBr_2$. The simplest method for the preparation of this salt is the solution of calcium carbonate in hydrobromic acid, an excess of the former being added, the mixture filtered when effervescence has ceased and the solution evaporated to dryness; a white granular powder is thus obtained, which is very deliquescent, and must be preserved in tightly stoppered bottles.

The Pharmacopœia demands practically absolute purity for this salt, by stating that 0.25 Gm. shall require 25 Cc. decinormal silver solution for complete precipitation. The equation, $CaBr_2 + 2AgNO_3 = 2AgBr + Ca(NO_3)_2$, shows that 199.46 parts of calcium bromide require 339.10 parts of silver nitrate, hence 25 Cc. $\frac{N}{10}$ $AgNO_3$ solution will precipitate 0.2492875 Gm. $CaBr_2$, which is 99.7 per cent. of 0.25 Gm.

Precipitated Calcium Carbonate. $CaCO_3$. This salt, popularly known as precipitated chalk, is prepared by double decomposition between calcium chloride and sodium carbonate; solutions of the two salts are mixed and heated, when calcium carbonate is thrown down as a dense precipitate while sodium chloride remains in solution. The decomposition may be illustrated as follows: $CaCl_2 + Na_2CO_3 = CaCO_3 + 2NaCl$; to remove the sodium chloride the mixture is poured on a strainer and the precipitate washed with boiling water until the washings no longer indicate the presence of chlorine.

If calcium carbonate be precipitated in the cold, it is flocculent and voluminous, in which condition it is difficult to wash it entirely free from the sodium chloride, hence the use of heat is advantageous. The precipitate consists of a micro-crystalline powder, entirely free, however, from grittiness.

It is not adapted for internal use, but is employed in the preparation of other calcium compounds.

PREPARED CHALK. $CaCO_3$. The compound officially recognized under the name prepared chalk is native soft calcium carbonate, freed by elutriation from most impurities. Chalk occurs abundantly, as a soft earthy mineral, on the English coast, which, by repeated treatment with water, may be gradually freed from impurities and coarser particles. The process of elutriation has been fully explained on page 104. After collecting the suspended fine powder, the latter, while still moist, is formed into small nodular masses by means of a funnel and then dried.

Chemically prepared chalk does not differ from the precipitated calcium carbonate, but, on account of its greater softness and adhesiveness, it is better adapted for internal administration, and is the kind of chalk used in the official chalk mixture and troches. Although it is never so white, and is probably less pure than the preceding article, the latter should never be used in its place.

CALCIUM CHLORIDE. $CaCl_2$. This compound is extensively obtained, in a crude state, as a by-product in different chemical processes. It may be obtained pure either by dissolving pure calcium carbonate in pure hydrochloric acid or by dissolving ordinary chalk or marble in hydrochloric acid and freeing the solution from iron and other impurities by treatment with chlorine and subsequently milk of lime; the mixture is warmed and filtered, the filtrate being finally exactly neutralized with hydrochloric acid.

If a concentrated solution of calcium chloride be set aside to crystallize, a salt of the composition $CaCl_2 + 6H_2O$, containing nearly 50 per cent. of water, will be obtained; but if the solution be evaporated until a granular powder results, a very deliquescent white salt of the composition $CaCl_2 + 2H_2O$, containing about 25 per cent. of water, is produced. The Pharmacopœia recognizes only the anhydrous salt, which requires for its preparation a temperature above 200° C. (392° F.), perfect fusion not occurring much below a red heat. The official salt is very deliquescent and must be preserved in tightly stoppered bottles.

Anhydrous calcium chloride is employed in pharmacy chiefly as a desiccating agent, while the crystallized salt is used as a reagent in analytical chemistry.

CALCIUM HYPOPHOSPHITE. $Ca(PH_2O_2)_2$. This salt, the parent salt of numerous other hypophosphites, is prepared by the direct action of phosphorus on calcium hydroxide in the form of milk of lime, phosphine, or hydrogen phosphide, being generated at the same time; $3Ca(OH)_2 + 6H_2O + P_8 = 3Ca(PH_2O_2)_2 + 2PH_3$. In order to avoid the formation of the very annoying and spontaneously inflammable phosphine as far as possible, E. Scheffer, as far back as

1858, advocated the use of partially oxidized phosphorus, prepared by treating it under water with atmospheric air, whereby the phosphorus is changed to a spongy condition and combines more readily with lime, even at the ordinary temperature, but preferably if the mixture be heated to 55° C. (131° F.). When the reaction has ended, the mixture is filtered, the residue washed with water, and the united filtrates evaporated and either granulated or allowed to crystallize.

Calcium hypophosphite is not hygroscopic, like the corresponding salts of potassium and sodium, and is very nearly as soluble in cold as in boiling water. The official salt should contain at least 99.68 per cent. of pure $Ca(PH_2O_2)_2$, which is determined with decinormal potassium permanganate solution, as already explained under potassium hypophosphite (which see). In the official test, the addition of sulphuric acid to the solution of the calcium salt precipitates calcium sulphate, liberating at the same time hypophosphorous acid, which is then oxidized by the permanganate solution and converted into phosphoric acid. The reactions may be indicated thus: $5Ca(PH_2O_2)_2 + 5H_2SO_4 = 5CaSO_4 + 10HPH_2O_2$ and $10HPH_2O_2 + 8KMnO_4 + 12H_2SO_4 = 10H_3PO_4 + 4K_2SO_4 + 8MnSO_4 + 12H_2O$, from which it may be seen that 1261.36 parts of potassium permanganate are required to oxidize the hypophosphorus acid obtainable from 848.35 parts of calcium hypophosphite; one Cc. $\frac{N}{10}$ $KMnO_4$ solution corresponds, therefore, to 0.0021208 Gm. of pure $Ca(PH_2O_2)_2$, hence 0.1 Gm. of the official salt, containing 0.009968 Gm. (99.68 per cent.) $Ca(PH_2O_2)$, will decolorize 47 Cc. $\frac{N}{10}$ $KMnO_4$ solution.

Precipitated Calcium Phosphate. $Ca_3(PO_4)_2$. Tricalcium phosphate may be obtained by digesting calcined bone with hydrochloric acid, whereby acid calcium phosphate and calcium chloride are formed, both of which remain in solution, and, upon addition of ammonia, are converted into tricalcium phosphate and ammonium chloride, the former being precipitated and freed from the latter by repeated washing with water. The different steps in the process may be illustrated by the following equations: $Ca_3(PO_4)_2 + 4HCl = CaH_4(PO_4)_2 + 2CaCl_2$ and $CaH_4(PO_4)_2 + 2CaCl_2 + 4NH_4OH = Ca_3(PO_4)_2 + 4NH_4Cl + 4H_2O$. If the precipitation is effected in a cold solution, the resulting product will be more voluminous but less readily freed from accompanying impurities than if hot solutions are used. Precipitated calcium phosphate may also be obtained by adding a solution of calcium chloride and ammonia water to a solution of sodium phosphate, when the following reaction will occur: $3CaCl_2 + 2NH_4OH + 2Na_2HPO_4 = Ca_3(PO_4)_2 + 2NH_4Cl + 4NaCl + 2H_2O$.

The calcium phosphate of the German Pharmacopœia differs from that of the United States and British Pharmacopœias in being secondary calcium phosphate, $CaHPO_4$, obtained by decomposition of calcium chloride with sodium phosphate; it is a crystalline powder and contains about 25 per cent. of water, having the formula $CaHPO_4 + 2H_2O$.

DRIED CALCIUM SULPHATE. The terms dried gypsum and calcined plaster are also applied to this compound, which is obtained by carefully heating native crystalline calcium sulphate, or gypsum, $CaSO_4 + 2H_2O$, until deprived of about three-fourths of its water. The heat must be carefully regulated and not allowed to exceed 105° C. (221° F.), as above this temperature the last portions of water will be expelled and the compound become anhydrous. If heated to 200° C. (392° F.), gypsum loses its property of uniting with water and setting to a firm mass, thus becoming useless for surgical purposes.

The official dried gypsum is a powder containing about 95 per cent. of calcium sulphate and 5 per cent. of water. It must be carefully protected from moisture.

LIME. CaO. Calcium oxide, better known as unslaked or caustic lime, is obtained by calcining calcium carbonate in suitable furnaces known as lime-kilns. Oyster-shells, limestone, marble, and other varieties of carbonate are used for the purpose, the final product varying in quality according to the source; for pharmaceutical and chemical purposes, lime obtained by calcination of white marble is the most desirable, being less contaminated with impurities.

Good lime occurs in hard but porous masses, which, upon addition of half their weight of water, become heated, and are converted into a soft white powder, known as slaked lime. The change is of a chemical nature, as is evidenced by the development of heat, resulting in the formation of calcium hydroxide, thus: $CaO + H_2O = Ca(OH)_2$. Since lime, upon exposure to air, gradually absorbs moisture, and finally carbon dioxide, it must be preserved in well-closed vessels in a dry place. Lime thus changed by exposure is called air-slaked lime.

Lime is used in pharmacy as a dehydrating agent and for the preparation of the official solution and syrup of lime. When slaked and mixed with five or six times its weight of water it forms a mixture known as milk of lime.

CHLORINATED LIME. This compound, which owes its value entirely to the amount of available chlorine it contains, is prepared by exposing slaked lime to the action of chlorine gas. The views held by chemists regarding the nature of the compound formed differ, and the question has, at the present day, not yet been settled. Some contend that calcium hypochlorite, calcium chloride, and water are produced, according to the equation $2Ca(OH)_2 + Cl_4 = Ca(ClO)_2 + CaCl_2 + 2H_2O$, while others regard the dry product as having the composition $CaOCl_2$, or $CaClOCl$, which, upon the addition of water, breaks up into calcium hypochlorite and chloride. The preponderance of opinion, at present, is in favor of the latter view, partly because the richest commercial samples of chlorinated lime or bleaching powder thus far produced do not contain the proportion of available

chlorine (about 49 per cent.), which the compound $Ca(ClO)_2 + CaCl_2 + 2H_2O$ should yield.

The term "chloride of lime," usually applied to this substance in commerce, is a misnomer, probably given to it long before the chemical nature of the manufacturing process was understood.

Chlorinated lime always contains some calcium hydroxide, to which its partial insolubility in water is due. It should always be kept in a cool, dry place, and protected from light, since the latter has a deleterious effect upon it, causing a loss of chlorine and oxygen with production of calcium chlorate and chloride. If of good quality, chlorinated lime is not deliquescent, the latter phenomenon indicating decomposition.

Solutions of chlorinated lime should always be prepared, without heat, by triturating the powder in a mortar with successive portions of water and rapidly filtering through paper or cotton.

The Pharmacopœia requires that the official product shall contain at least 35 per cent. of available chlorine, which may be determined, as in the case of chlorinated soda, by treatment with hydrochloric acid and potassium iodide and subsequent titration of the liberated iodine with sodium thiosulphate. When hydrochloric acid is added to chlorinated lime, the following decomposition takes place: $2Ca(ClO)Cl$ or $(Ca(ClO)_2 + CaCl_2) + 4HCl = Cl_4 + 2CaCl_2 + 2H_2O$. The action of nascent chlorine on potassium iodide has been explained on page 409, and, from the amount of decinormal sodium thiosulphate solution used to decolorize the iodine solution, the weight of liberated chlorine can be calculated. Each Cc. $\frac{N}{10}$ $Na_2S_2O_3$ solution corresponds to 0.003537 Gm. of chlorine, therefore 35 Cc. will be necessary to indicate 0.1225 Gm. (35 per cent. of 0.35 Gm.), for $0.003537 \times 35 = 0.123795$.

Sulphurated Lime. The official process for this preparation consists in heating a mixture of 70 parts of dried calcium sulphate, 10 parts of charcoal, and 1 part of starch, in a loosely covered crucible, to bright redness, until a uniform gray color results. The reaction consists in the reduction of calcium sulphate to sulphide and the formation of carbon monoxide and dioxide, which escape, thus: $CaSO_4 + C_3 = CaS + 2CO + CO_2$. The starch simply aids in the reduction, which, however, is not complete, as the finished product contains unchanged calcium sulphate and carbon in varying proportions.

Sulphurated lime, being liable to decomposition when exposed to air, must be carefully preserved in air-tight vessels. The official article is required to contain at least 60 per cent. of calcium monosulphide, upon which the virtues of the preparation depend; the determination being made by adding 1 Gm. of sulphurated lime to a boiling solution of 2.08 Gm. of crystallized cupric sulphate, when the copper should be completely precipitated as sulphide. The equation, $CuSO_4.5H_2O + CaS = CuS + CaSO_4 + 5H_2O$, shows that

248.8 parts of crystallized cupric sulphate require 71.89 parts of calcium monosulphide, hence 2.08 Gm. will require 0.601 Gm., which is practically 60 per cent. of 1 Gm.

SOLUTION OF LIME. This liquid, more familiarly known as lime-water, is intended to be a saturated solution of calcium hydroxide. The official directions for its preparation are simple and easily followed, the object of rejecting the first solution obtained after half an hour's maceration of the slaked lime with water being to get rid of the more soluble impurities, after which the purified lime is kept in contact with water as long as it continues to furnish a saturated solution. It must not be supposed, however, that lime will furnish unlimited quantities of lime-water, and the supply should be tested from time to time, either volumetrically, as directed by the Pharmacopœia, or empirically, by breathing into a small quantity of it through a glass tube or boiling a little of it in a test-tube—in either case a turbid liquid should result, due to the separation of calcium carbonate in the first place, or calcium hydroxide in the second.

Lime-water is a very important article in pharmacy, and should receive careful attention, as it is chiefly used as an antacid for delicate infants. Pure lime, free from alum, should be used, and either distilled water, or that which has been boiled and cooled. The supply of lime-water should be kept in tightly corked bottles, in a cool place, as carbon dioxide is readily absorbed and heat is unfavorable to solution of the lime. Lime-water is best decanted from the sediment—or, if filtered, this must be done under cover —the sediment should then be again well distributed in the liquid, by agitation, after the desired supply of solution has been withdrawn.

While a saturated aqueous solution of lime, at 15° C. (59° F.), contains about 1.70 or 1.75 Gm. of calcium hydroxide in every liter, the official requirement of 1.40 or 1.48 Gm. per liter more nearly represents the average strength of good lime-water. According to the equation, $(H_2C_2O_4 + 2H_2O) + Ca(OH)_2 = CaC_2O_4 + 4H_2O$, each Cc. of decinormal oxalic acid solution, containing 0.006285 Gm. of oxalic acid, will neutralize 0.003691 Gm. of calcium hydroxide, hence, if 50 Cc. of lime-water require 20 Cc. $\frac{N}{10}$ $H_2C_2O_4$ solution, as stated in the official test, about 0.07382 Gm. $Ca(OH)_2$ is present, which is equal to about 0.140–0.1476 per cent.

SYRUP OF LIME. This preparation contains a much larger proportion of lime in solution than lime-water, owing to the presence of sugar, and is, therefore, preferred in some cases. It has also been recommended as an antidote in cases of poisoning by carbolic acid, and is said to have been used with good results. As already stated on page 224, syrup of lime, when freshly prepared, contains about 3.2 Gm. of lime, CaO, in every 100 Cc. (about 16 grains in 1 fluidounce); as it absorbs carbon dioxide rapidly from the air, it must be carefully

preserved, and, when filtration is necessary, as in its preparation, covered funnels only should be used.

The saccharated solution of lime of the British Pharmacopœia is a similar preparation, but contains only about one-half as much calcium oxide in solution.

SYRUP OF CALCIUM LACTOPHOSPHATE. This syrup has already been fully considered on page 224.

The Compounds of Strontium.

STRONTIUM BROMIDE. $SrBr_2 + 6H_2O$. This salt may be prepared by neutralizing diluted hydrobromic acid with pure strontium carbonate added in excess, filtering the mixture, and evaporating the solution until crystals begin to form. Upon cooling, the salt separates in crystals which should be dried at a moderate heat.

Since pure strontium carbonate is difficult to obtain, the use of pure strontium hydroxide has been suggested instead, as the latter may be prepared readily from the nitrate by converting it into oxide by calcination and then slaking this with water, removing any barium and calcium present by further appropriate treatment with water.

The official salt contains about 30.4 per cent. of water of crystallization, and deliquesces rapidly upon exposure to air. It can be rendered anhydrous by heating to 120° C. (248° F.), and, in that condition, should contain not less than 98 per cent. of absolute $SrBr_2$, as determined by means of decinormal silver nitrate solution, the reaction being identical with that explained under Potassium Bromide (see page 434). 0.3 Gm. of anhydrous absolute strontium bromide require 24.32 Cc. $\frac{N}{10}$ $AgNO_3$ solution for complete precipitation, while 0.3 Gm. of absolute strontium chloride require 37.21 Cc.; hence, each 0.1289 Cc. required in excess of 24.32 Cc. will indicate 1 per cent. of chloride present. In the official test, 24.6 Cc. $\frac{N}{10}$ $AgNO_3$ solution are allowed, which will indicate practically 2 per cent. of chloride; for $24.6 - 24.32 = 0.28$ and $0.28 \div 0.1289 = 2.17$.

STRONTIUM IODIDE. $SrI_2 + 6H_2O$. Like strontium bromide, this salt may be prepared either from pure strontium carbonate or hydroxide by solution in the respective acid, but, since solution of hydriodic acid is rather unstable, it should be freshly prepared for the purpose. The process is identical with that for the preceding salt.

Strontium iodide is also deliquescent but contains less water of crystallization (24.05 per cent.) than the bromide. By exposure to air and light it is colored yellow, and must, therefore, be preserved in dark, amber-colored bottles.

The Pharmacopœia requires that at least 98 per cent. pure stron-

tium iodide shall be contained in the anhydrous salt. Since not more than 18 Cc. of decinormal silver nitrate solution shall be required for precipitation of 0.3 Gm. of the anhydrous salt, 0.73 Cc. is allowed for possible admixture of bromide and chloride, because 0.294 Gm. (98 per cent. of 0.3) of absolute strontium iodide require only 17.27 Cc. of the silver solution.

STRONTIUM LACTATE. $Sr(C_3H_5O_3)_2 + 3H_2O$. Strontium lactate is made by neutralizing moderately dilute lactic acid with strontium carbonate or hydroxide and evaporating the resulting solution to dryness with a moderate heat. The salt is not deliquescent.

The nature of the compound, as regards the acid radical present, is determined by treating a 5 per cent. solution of the salt with potassium permanganate in the presence of sulphuric acid, as directed in the Pharmacopœia. The decoloration of the red permanganate solution, together with effervescence of the mixture and development of an aldehyde odor, is due to oxidation of the lactic acid, which is first liberated from the salt by sulphuric acid. Under the influence of oxidizing agents, lactic acid breaks up into acetic aldehyde, C_2H_4O, and formic acid, $HHCO_2$, the latter being still further oxidized to carbon dioxide and water.

The official salt, having been rendered anhydrous, should contain not less than 98.6 per cent. of pure strontium lactate, which is determined by converting it into carbonate by means of ignition and then titrating the carbonate with normal acid. 1.33 Gm. of anhydrous strontium lactate will yield, upon ignition, 0.73886 Gm. of strontium carbonate, as shown by the equation, $Sr(C_3H_5O_3)_2 + O_{12} = SrCO_3 + 5CO_2 + 5H_2O$, and, as each Cc. $\frac{N}{1}$ H_2SO_4 requires 0.073886 Gm. $SrCO_3$ for neutralization, it will correspond to 0.13244 Gm. anhydrous strontium lactate; hence, 9.9 Cc. will be required to show 98.6 per cent. of 1.33 Gm., for $0.13244 \times 9.9 = 1.311 +$ and 98.6 per cent. of 1.33 is 1.311 +.

CHAPTER XLV.

THE COMPOUNDS OF MAGNESIUM.

ALTHOUGH the official magnesium salts are but few in number they are extensively employed both by physicians and in domestic practice. The Pharmacopœia recognizes six preparations of magnesium, of which one is a liquid. The following comprise the list:

Official English Name.	Official Latin Name.
Magnesia,	Magnesia.
Heavy Magnesia,	Magnesia Ponderosa.
Magnesium Carbonate,	Magnesii Carbonas
Effervescent Magnesium Citrate,	Magnesii Citras Effervescens.
Magnesium Sulphate,	Magnesii Sulphas
Solution of Magnesium Citrate,	Liquor Magnesii Citratis.

MAGNESIA. MgO. The name, calcined magnesia, by which this compound is commonly known, indicates the manner of its preparation. Magnesium carbonate is pressed somewhat firmly into a crucible and then heated to dull redness, whereby carbon dioxide and water are expelled, leaving about 42 per cent. of residue consisting of magnesium oxide. The process is known to be completed when a small quantity of the residue, suspended in water, no longer effervesces upon addition of an acid. The heat is not allowed to rise to full redness unless the powder can be kept constantly stirred, otherwise the magnesia is very apt to become granular. The following equation illustrates the change taking place: $(4MgCO_3 + Mg(OH)_2 + 5H_2O) = 5MgO + 4CO_2 + 6H_2O$.

Two varieties, a light and a dense calcined magnesia, occur in commerce; the latter is recognized in the Pharmacopœia as heavy magnesia, or magnesia ponderosa. The two varieties are obtained in the same manner, but from light and heavy magnesium carbonate, respectively. Light magnesia is the kind generally used, and should invariably be employed when magnesia is to be dispensed in aqueous suspension; small quantities of water cannot be mixed with it without rendering it harsh and gritty, and, if 1 part of magnesia be added to 15 parts of water, the mixture will soon set to a gelatinous mass, hence care must be observed that sufficient water be used to overcome this tendency, and never should the water be added to the magnesia, but always the magnesia to the water. This peculiar behavior with water is due to the formation of gelatinous magnesium hydroxide $Mg(OH)_2$, and is characteristic of the light magnesia, heavy magnesia not readily uniting with water.

Light and heavy magnesia do not differ from each other chemi-

cally; the latter is a smoother and denser powder, preferred for use in powder mixtures on account of its smaller bulk.

Since magnesia absorbs moisture and carbon dioxide readily from the air, it must be preserved in tightly closed tin or glass vessels. The Pharmacopœia demands that only slight traces of carbonate shall be present, and not more than 5 per cent. of moisture.

MAGNESIUM CARBONATE. $4MgCO_3 + Mg(OH)_2 + 5H_2O$. As shown by the chemical formula, the official magnesium carbonate is not a pure normal carbonate, but is composed of magnesium carbonate and hydroxide united with water. It is prepared by mutual decomposition between solutions of magnesium sulphate or chloride, and of sodium carbonate; the composition of the resulting precipitate depends upon the concentration of the solutions employed and the temperature at which the decomposition is effected, and the precipitate dried. Pure normal magnesium carbonate is never obtained when a solution of the sulphate or chloride is mixed with an alkali carbonate, but always a basic carbonate, the proportion of normal carbonate present in the precipitate being greatest, when dilute solutions are used at ordinary temperature.

If solutions of magnesium sulphate and sodium carbonate be mixed in the cold, no carbon dioxide is eliminated, a voluminous precipitate of basic magnesium carbonate being thrown down, while an acid magnesium carbonate, $MgH_2(CO_3)_2$, remains in solution; but, if the solutions be mixed warm or hot, carbon dioxide is evolved. The reaction producing the official magnesium carbonate is probably as follows: $5(MgSO_4 + 7H_2O) + 5(Na_2CO_3 + 10H_2O) = (4MgCO_3 + Mg(OH)_2 + 5H_2O) + 5Na_2SO_4 + CO_2 + 79H_2O$, dilute solutions being used and mixed at a temperature not above 55° C. (131° F.); the precipitate is washed to remove sodium chloride, and dried without heat.

Both light and heavy magnesium carbonate occur in commerce, being manufactured extensively in this country and in England. The U. S. Pharmacopœia recognizes only the light variety, as indicated by the official description; this is also known as *magnesia alba*. The British Pharmacopœia recognizes both the light and heavy magnesium carbonate and gives working formulas for their preparation, which differ from each other only in the concentration of the solutions used and in the length of time the mixture is boiled; the official English magnesium carbonate has the composition, $3MgCO_3 + Mg(OH)_2 + 4H_2O$.

Considerable magnesium carbonate is also made in England from dolomite, a native magnesium limestone, by ignition and treatment with water and carbon dioxide under pressure; acid magnesium carbonate is formed and readily dissolved, and the solution, separated from the calcium carbonate, is treated with steam, whereby the basic carbonate is precipitated.

[illegible]

[illegible] The normal citrate, [illegible] slightly soluble in [illegible] 14 molecules, or about [illegible] crystalline precipitate [illegible] citrate, and is formed when- [illegible] and 1.44 parts of citric acid are [illegible] Acid magnesium citrate, $MgHC_6H_5O_7$, requires

2.16 parts of citric acid for each part of magnesium carbonate used; it is very soluble in water, but is objected to by many on account of its very acid taste.

By following the official formula, a mixture of normal and acid magnesium citrate is produced, as insufficient citric acid is used to form the latter salt alone. Since 2.5 Gm. of potassium bicarbonate require about 1.75 Gm. of citric acid for complete decomposition, and only 0.6 Gm. are furnished by the 60 Cc. of syrup of citric acid ordered, there will be still less acid magnesium citrate in the finished product and the tendency to deposit the normal salt will be increased. The first edition of the 1890 Pharmacopœia directed 120 Cc. of syrup of citric acid, but this was changed afterward, as the solution was found too sweet, containing about 100 Gm. of sugar in every bottle. For extemporaneous preparation of solution of magnesium citrate, the pharmacopœial formula answers admirably and the citric acid may even be reduced to 25 Gm., with advantage as regards the taste; but, if the solution is to be kept in bottles, for possibly a week or two or even longer, a more acid solution should be prepared, using 33.58 Gm. of citric acid in place of 30 Gm., as officially directed.

Another source of trouble is the use of plain water, which sometimes causes fungi to form and renders the solution unsightly; this can be obviated by boiling and filtering all the water to be used. Sound soft corks only should be used for closing the bottles, and, having been first swelled in water for an hour, they should be driven firmly into the neck of the bottle and then secured with twine or wire, as retention in the solution of all the carbon dioxide, from the potassium bicarbonate, adds materially to the refreshing taste. The bottles should be kept in a cool place, resting on their sides.

CHAPTER XLVI.

THE COMPOUNDS OF ALUMINUM AND CERIUM.

There are but four compounds of aluminum and one of cerium recognized in the Pharmacopœia, as shown by the following list:

Official English Name.	Official Latin Name.
Alum,	Alumen.
Dried Alum,	Alumen Exsiccatum.
Aluminum Hydrate.	Alumini Hydras.
Aluminum Sulphate.	Alumini Sulphas.
Cerium Oxalate,	Cerii Oxalas.

The Compounds of Aluminum.

ALUM. $Al_2K_2(SO_4)_4 + 24H_2O$. In pharmacy and medicine the term alum is applied to but one compound, although chemists recognize under the general name of alum several definite salts, the characteristics of which are, that they are double sulphates of a univalent and trivalent element, are isomorphous, crystallizing in the regular system of the cube and octahedron, and contain 24 molecules of water of crystallization. The univalent elements present may be either potassium, sodium, ammonium, cæsium, rubidium, or silver, while the trivalent element need not necessarily be aluminum, its place being sometimes taken by iron, chromium, or manganese. The official alum is designated more specifically as potassium alum; besides this, the following are also known: ammonium alum, $Al_2(NH_4)_2(SO_4)_4 + 24H_2O$; chrome alum, $Cr_2K_2(SO_4)_4 + 24H_2O$; iron alum, $Fe_2(NH_4)_2(SO_4)_4 + 24H_2O$, etc., etc.

Crude alum occurs in Nature in the form of alunite or alumstone, a mixture of aluminum hydroxide and aluminum and potassium sulphates; from this as well as alum-shale and the minerals cryolite and bauxite official alum is obtained. Calcination and lixiviation, as well as treatment with sulphuric acid and addition of potassium sulphate or chloride, are brought into requisition in the different processes, crystallization being finally employed for the purpose of purification. Owing to the presence of iron in the minerals from which alum is made, it is often found in the latter, but should not exceed traces, as determined by the official test with potassium ferrocyanide.

Potassium alum is not quite so soluble as ammonium alum, which latter was formerly recognized in the Pharmacopœia, and is still

more extensively handled in commerce than the official article, partly on account of its lower price. The British Pharmacopœia recognizes both varieties. Ammonium alum may be readily distinguished from the official alum by the evolution of an ammoniacal odor upon trituration with potassium or sodium hydroxide or carbonate; moreover, upon heating, ammonium alum leaves a final residue of pure alumina, while the residue from official alum contains potassium sulphate besides.

DRIED ALUM. $Al_2K_2(SO_4)_4$. Crystallized potassium alum contains 45.52 per cent. of water of crystallization, which may be entirely expelled at a temperature of 200° C. (392° F.). In the official process for preparing dried or burnt alum, the crystals are first fused in a shallow capsule, the heat being then increased and continued until 10 parts have been reduced in weight to 5.5 parts and a white porous mass remains, which is preserved in powder form in tightly stoppered bottles. A temperature exceeding 200° C. (392° F.) must be avoided to prevent decomposition and change of the aluminum sulphate to alumina, with loss of sulphuric acid.

Dried alum, although completely but slowly soluble in water, requires about three or four times as much water for solution as the crystallized alum.

ALUMINUM HYDRATE OR HYDROXIDE. $Al_2(OH)_6$ or $Al(OH)_3$. The Pharmacopœia directs this compound to be prepared by gradually pouring a hot solution of alum into a hot solution of an equal weight of sodium carbonate, repeatedly washing the resulting precipitate with hot water, and finally drying the residue at a temperature not above 40° C. (104° F.). The decomposition is accompanied by the evolution of carbon dioxide, and may be illustrated as follows: $3Na_2CO_3 + Al_2K_2(SO_4)_4 + 3H_2O = Al_2(OH)_6 + K_2SO_4 + 3Na_2SO_4 + 3CO_2$; this peculiar reaction is characteristic of certain metals, aluminum, iron in the ferric state, and chromium, the oxides of which exhibit weak basic properties and fail to combine with carbonic acid, but are precipitated as hydroxides when their soluble salts are acted upon by alkali carbonates.

The object of using hot solutions of the two salts and of adding the alum solution slowly to the alkaline liquid is to prevent the formation of basic aluminum sulphate and to facilitate the complete removal of alkali and sulphuric acid, which would be persistently retained by the precipitated hydroxide if the precipitation took place in the presence of an excess of alum. The use of hot liquids also facilitates the elimination of the carbon dioxide.

Drying the precipitate at a moderate temperature is desirable to insure a smooth product, as a high heat would cause partial decomposition and a gritty powder.

ALUMINUM SULPHATE. $Al_2(SO_4)_3 + 16H_2O$. This salt is preferably prepared for medicinal purposes by dissolving freshly prepared

aluminum hydroxide in a sufficient quantity of sulphuric acid properly diluted with water. An excess of acid should be avoided, as also an excess of the hydroxide; in the event of the latter, basic sulphates are likely to be formed. 100 Gm. of aluminum hydroxide (obtained from 607.33 Gm. of official alum) require 188.31 Gm. of absolute, or 203.58 Gm. of official sulphuric acid to form a normal salt. The gelatinous hydroxide will dissolve quite readily, and the solution having been filtered is evaporated on a water-bath until a crystalline residue is obtained.

Aluminum sulphate contains about the same percentage of water of crystallization as official alum, but is far more soluble (about 8 times) than the latter.

Besides the official aluminum compounds the following is sometimes used:

SOLUTION OF ALUMINUM ACETATE. This preparation is recognized in the German Pharmacopœia, and is prepared by adding 360 Gm. of 30 per cent. acetic acid to a solution of 300 Gm. of aluminum sulphate in 800 Cc. of water, and afterward introducing, in small portions at a time, a mixture of 130 Gm. of calcium carbonate in 200 Cc. of water. The whole operation must be conducted in a cool place and the mixture be allowed to stand at rest for 24 hours, when the clear liquid may be removed with the aid of a siphon. The solution contains about 7.5 or 8 per cent. of basic aluminum acetate of the composition, $Al_2(OH)_2(C_2H_3O_4)_4$. The reaction taking place in the foregoing process may be illustrated thus: $(Al_2(SO_4)_3 + 16H_2O) + 4HC_2H_3O_2 + 3CaCO_3 = Al_2(OH)_2(C_2H_3O_2)_4 + 3CaSO_4 + 3CO_2 + 17H_2O$.

The Compounds of Cerium.

CERIUM OXALATE. $Ce_2(C_2O_4)_3 + 9HO_2$. This salt is prepared from the mineral cerite by a somewhat complicated process, on account of the presence of two other metals, lanthanum and didymium, which are intimately associated with cerium as silicates. The powdered mineral is digested with sulphuric acid, the mass dried and treated with diluted nitric acid and hydrogen sulphide to remove copper and other metals. The cerite metals are next precipitated by means of oxalic acid, and the mixed oxalates, after the addition of magnesium carbonate, are calcined and the residue dissolved in a small quantity of concentrated nitric acid. The solution is poured into a large quantity of water containing about one-half per cent. of sulphuric acid, whereby the cerium is precipitated as yellow ceric sulphate, while lanthanum and didymium, together with the magnesium, remain in solution. The ceric sulphate is dissolved in sulphuric acid and reduced to cerous sulphate, by means of sodium

thiosulphate, after which it is precipitated, as cerous oxalate, with oxalic acid and dried.

Pure cerium oxalate is white, but the commercial article is frequently of a pink color, due to the presence of didymium, which may be detected by heating the suspected salt to redness, when a reddish-yellow residue of ceric oxide should be obtained, didymium imparting a brown color, as stated in the official test.

Among the non-official salts of cerium, the nitrate, $Ce(NO_3)_3 + 6H_2O$, has been used to some extent. It may be conveniently made by decomposing cerous sulphate with barium nitrate, and possesses the advantage of being freely soluble in water and alcohol.

CHAPTER XLVII.

THE COMPOUNDS OF IRON.

THERE is no class of inorganic compounds, excepting the official preparations of the alkalies, more extensively employed in medicine than those of iron; they must therefore be considered as among the most important in the study of pharmacy. The Pharmacopœia recognizes, besides iron in the metallic form, no less than 38 different preparations of the same, of which 12 are liquid. Chemists have grouped all compounds of iron into two classes, designated as ferrous and ferric compounds respectively, which differ from each other in striking physical and chemical properties; this distinction has also been maintained in the official titles of the iron salts and their solutions. Ferrous compounds, in which iron is bivalent, are, when not anhydrous, of a green color, with one exception, the yellow oxalate, and form a blue precipitate of ferrous ferricyanide, $Fe_3(Fe(CN)_6)_2$, known as Turnbull's Blue, with solution of potassium ferricyanide; ferric compounds, in which iron is trivalent, on the other hand, are characterized by a reddish- or yellowish-brown color and form a blue precipitate of ferric ferrocyanide, $Fe_4(Fe(CN)_6)_3$, known as Prussian Blue, with solution of potassium ferrocyanide.

The following is a list of the official preparations of iron, divided, for convenience, into three classes:

Official English Name.	Official Latin Name.
Metallic Iron.	
Iron,	Ferrum.
Reduced Iron,	Ferrum Reductum.
Ferrous Compounds.	
Ferrous Sulphate,	Ferri Sulphas.
Dried Ferrous Sulphate,	Ferri Sulphas Exsiccatus.
Granulated Ferrous Sulphate,	Ferri Sulphas Granulatus.
Mass of Ferrous Carbonate,	Massa Ferri Carbonatis.
Saccharated Ferrous Carbonate,	Ferri Carbonas Saccharatus.
Pills of Ferrous Carbonate,	Pilulæ Ferri Carbonatis.
Ferrous Lactate,	Ferri Lactas.
Pills of Ferrous Iodide,	Pilulæ Ferri Iodidi.
Saccharated Ferrous Iodide,	Ferri Iodidum Saccharatum.
Syrup of Ferrous Iodide,	Syrupus Ferri Iodidi.
Compound Iron Mixture,	Mistura Ferri Composita.
Ferric Compounds.	
Ferric Ammonium Sulphate,	Ferri et Ammonii Sulphas.
Ferric Chloride,	Ferri Chloridum.
Ferric Citrate,	Ferri Citras.
Ferric Hydrate,	Ferri Oxidum Hydratum.

Ferric Hydrate with Magnesia,	Ferri Oxidum Hydratum cum Magnesia.
Ferric Hypophosphite,	Ferri Hypophosphis.
Ferric Valerianate,	Ferri Valerianas.
Iron and Ammonium Citrate,	Ferri et Ammonii Citras.
Iron and Ammonium Tartrate,	Ferri et Ammonii Tartras.
Iron and Potassium Tartrate,	Ferri et Potassii Tartras.
Iron and Quinine Citrate,	Ferri et Quininæ Citras.
Soluble Iron and Quinine Citrate,	Ferri et Quininæ Citras Solubilis.
Iron and Strychnine Citrate.	Ferri et Strychninæ Citras.
Soluble Ferric Phosphate,	Ferri Phosphas Solubilis.
Soluble Ferric Pyrophosphate,	Ferri Pyrophosphas Solubilis.
Solution of Ferric Acetate,	Liquor Ferri Acetatis.
Solution of Ferric Chloride,	Liquor Ferri Chloridi.
Solution of Ferric Citrate,	Liquor Ferri Citratis.
Solution of Ferric Nitrate,	Liquor Ferri Nitratis.
Solution of Ferric Subsulphate,	Liquor Ferri Subsulphatis.
Solution of Ferric Sulphate,	Liquor Ferri Tersulphatis.
Solution of Iron and Ammonium Acetate,	Liquor Ferri et Ammonii Acetatis.
Tincture of Ferric Chloride,	Tinctura Ferri Chloridi.
Iron Plaster,	Emplastrum Ferri.
Troches of Iron,	Trochisci Ferri.
Bitter Wine of Iron,	Vinum Ferri Amarum.
Wine of Ferric Citrate,	Vinum Ferri Citratis.

IRON. Fe. The kind of metallic iron recognized in the Pharmacopœia is that occurring in the form of soft, bright wire. It should be free from rust and the commercial article, as it has usually been coated with grease or paraffin oil to protect it from moisture, must be thoroughly cleaned before it is used for pharmaceutical purposes. The kind of iron wire known in the trade as card-teeth, obtained as clippings and waste from the manufacturers of cotton cards, is usually preferred on account of its convenient form and general good quality; sometimes, however, card-teeth of a very inferior grade are sold and require careful garbling and subsequent washing to remove grease and dirt.

REDUCED IRON. This preparation represents more or less pure metallic iron in a fine state of division, obtained by reduction of ferric oxide with hydrogen gas. Ferric hydroxide (see Ferric Hydrate) is first dried, whereby it is changed to oxyhydrate, and then placed in an iron reduction tube so arranged that the same can be heated to dull redness, while a current of hydrogen gas, previously washed and dried by being passed through a moderately strong solution of potassium permanganate and afterward sulphuric acid, is constantly passed through it. The reducing action of hydrogen on ferric oxide may be illustrated by the following equation: $Fe_2O_3 + H_6 = Fe_2 + 3H_2O$. The supply of hydrogen is kept up as long as any oxygen is left, as shown by the escape of aqueous vapor from the tube. When reduction is complete the tube and contents are allowed to cool slowly, while a slow stream of hydrogen is continued until the temperature has been reduced to that of the air; this is necessary, otherwise the hot, finely divided iron will be readily re-

oxidized by the air, as in that condition its avidity for oxygen is very marked.

The quality of reduced iron depends, of course, upon the purity of the ferric hydroxide and the temperature employed. When ferric oxide is heated to 280° or 300° C. (536°–572° F.) in a stream of hydrogen, it is converted into ferroso-ferric oxide, Fe_3O_4,($3Fe_2O_3 - H_2 = 2Fe_3O_4$ or $2(FeO - Fe_2O_3) - H_2O$), but metallic reduction does not occur until a temperature of 400° C. (752° F.) and over is reached. A bright red heat, however, is not employed, as it causes a dense, compact product, which is not desirable; therefore the commercial article, although a lighter powder, is usually contaminated with imperfectly reduced oxide.

Reduced iron should be free from lustre and of a grayish color, and, when treated with warm diluted sulphuric or hydrochloric acid, should leave not more than 1 per cent. of insoluble residue. Its value is based upon the proportion of metallic iron present; the U. S. Pharmacopœia demands 80 per cent., while the German Pharmacopœia insists upon 90 per cent. Frequent examinations of the commercial products have disclosed the fact that much inferior reduced iron is dispensed by pharmacists, but few samples coming up to the official requirements.

The Pharmacopœia directs that the valuation of reduced iron shall be made with mercuric chloride and potassium permanganate, the assay being subsequently confirmed by means of potassium iodide and sodium thiosulphate. The test involves several reactions, as follows: 1. When reduced iron is digested with solution of mercuric chloride, the latter salt is reduced to mercurous chloride by the metallic iron present, ferrous chloride being formed at the same time; thus, $2HgCl_2 + Fe = Hg_2Cl_2 + FeCl_2$. 2. Ferrous chloride, when treated with potassium permanganate and sulphuric acid, is converted into ferric sulphate and chloride; thus, $10\,FeCl_2 + 2KMnO_4 + 8H_2SO_4 = 2Fe_2(SO_4)_3 + 3Fe_2Cl_6 + 2KCl + 2MnSO_4 + 8H_2O$. 3. This mixture, digested with potassium iodide, liberates iodine, which is held in solution by the excess of potassium iodide, at the same time forming potassium sulphate and chloride, while the ferric salts are reduced to the ferrous state; thus, $2Fe_2(SO_4)_3 + 3Fe_2Cl_6 + 10KI = I_4 + 4FeSO_4 + 6FeCl_2 + 2K_2SO_4 + 6KCl$. These reactions plainly show that, for each atom (or 55.88 parts) of metallic iron present in the reduced iron, one atom (or 126.53 parts) of iodine is finally liberated, and, as each Cc. of decinormal sodium thiosulphate solution will decolorize 0.012653 Gm. of iodine, it must correspond also to 0.005588 Gm. of metallic iron. The second equation shows that 2 molecules of potassium permanganate are capable of oxidizing 10 molecules of ferrous salt, representing 10 atoms of iron; therefore each Cc. $\frac{N}{10}$ $KMnO_4$ solution, containing 0.0031534 Gm. $KMnO_4$, must correspond to 0.005588 Gm. of metallic iron.

In the official test, the 10 Cc. of filtrate directed to be used represent 0.056 Gm. of reduced iron, as 0.56 Gm. was used to obtain 100

Cc. of liquid, and each Cc $\frac{x}{10}$ $KMnO_4$ solution necessary to obtain a permanent pink coloration (showing complete oxidation) indicates 0.005588 Gm. or 10 per cent. of metallic iron; at least 8 Cc. will be required if the sample is of the quality officially required.

FERROUS SULPHATE. $FeSO_4+7H_2O$. This salt, from which numerous other ferrous as well as ferric compounds are made, is obtained, for medicinal purposes, by acting on clean iron wire with diluted sulphuric acid, aiding the reaction with a little heat. The newly formed ferrous sulphate enters into solution and hydrogen gas is eliminated, thus: $Fe_2+2H_2SO_4=2FeSO_4+H_4$; the salt is prone to oxidation if a strictly neutral solution be evaporated, hence a little free sulphuric acid is usually left in the liquid, which is then concentrated and crystallized.

The official ferrous sulphate contains 45.32 per cent. of water of crystallization, a portion of which is lost by efflorescence upon exposure to dry air; when exposed to moist air the salt undergoes oxidation, indicated by the formation of a brownish-yellow basic ferric sulphate. The crystals should therefore be preserved in well-stoppered bottles.

The commercial crude ferrous sulphate known as "copperas," is always more or less impure and not suited for pharmaceutical purposes. The Pharmacopœia requires absolute purity for the official salt, which is determined volumetrically with decinormal potassium permanganate solution. Each molecule of potassium permanganate is capable of converting 5 molecules of ferrous sulphate into ferric sulphate; thus, $10(FeSO_4+7H_2O)+2KMnO_4+8H_2SO_4=5Fe_2(SO_4)_3+K_2SO_4+2MnSO_4+78H_2O$; hence each Cc. $\frac{x}{10}$ $KMnO_4$ solution corresponds to 0.027742 Gm. of crystallized pure ferrous sulphate, and not less than 50 Cc. will be required for 1.39 Gm., as $1.39 \div 0.027742=50.1+$.

DRIED FERROUS SULPHATE. Approximately $2FeSO_4+3H_2O$. The Pharmacopœia directs dried ferrous sulphate to be prepared by allowing the crystallized salt to effloresce at a gentle heat and then exposing it in a dish to the heat of a boiling-water bath until reduced to about 65 per cent. of its original weight. This procedure does not render the salt anhydrous, for, even at 115° C. (239° F.) 6.48 per cent. of water still remains, which requires a heat of nearly 300° C. (592° F.) for complete expulsion; at the latter temperature the ferrous sulphate is likely to undergo decomposition.

Dried ferrous sulphate may be conveniently employed for pill-masses and other purposes, in place of the crystallized salt, in the proportion of 0.65 Gm. for 1 Gm. or (or 6.5 grains for 10 grains) of the latter.

GRANULATED FERROUS SULPHATE. $FeSO_4+7H_2O$. This salt differs from official ferrous sulphate in being in the form of a crystal-

line powder instead of large crystals, containing, however, the same amount of water. It is of a much paler color than the crystals, and, owing to its mode of preparation, is less liable to oxidation. The washing of the crystalline powder with alcohol is for the purpose of removing the acid and uncombined water as completely as possible, thus facilitating drying; a more effectual plan is to pour the acid solution, when cold, into one-half its volume of alcohol, whereby the salt is precipitated and can then be drained on a strainer and washed with diluted alcohol until free from acid. Rapid drying in direct sunlight is advantageous, as it prevents oxidation.

Granulated ferrous sulphate presents a convenient form for dispensing purposes.

MASS OF FERROUS CARBONATE. This preparation has already been considered on page 334, which see. The reaction occurring between the two solutions of ferrous sulphate and sodium carbonate may be illustrated thus: $(FeSO_4 + 7H_2O) + (Na_2CO_3 + 10H_2O) = FeCO_3 + Na_2SO_4 + 17H_2O$, showing that 277.42 parts of crystallized ferrous sulphate will yield 115.73 parts of ferrous carbonate; 100 Gm., therefore, should yield about 42 Gm. if none of the precipitate be lost, as 277.42 : 115.73 :: 100 : 41.71. The object of the addition of syrup to the iron solution and subsequent washing of the precipitate with sweetened water is to prevent oxidation of the iron salt, as far as possible.

SACCHARATED FERROUS CARBONATE. Although but little used at the present time, this preparation is still recognized in the Pharmacopœia. It closely resembles the preceding preparation, except that it occurs in powder form and is directed to contain a minimum limit of ferrous carbonate. The official directions are to pour a hot solution of 50 Gm. of ferrous sulphate into a warm solution of 35 Gm. of sodium bicarbonate contained in a flask, aiding decomposition by rotating the vessel. The precipitate is repeatedly washed with hot water until the newly formed sodium sulphate has been removed, after which the precipitate is drained, mixed with 80 Gm. of sugar, evaporated to dryness, reduced to powder, and incorporated with sufficient sugar to make the finished product weigh 100 Gm. The reaction differs from that stated above in being accompanied by evolution of carbon dioxide; thus, $(FeSO_4 + 10H_2O) + 2NaHCO_3 = FeCO_3 + Na_2SO_4 + CO_2 + 11H_2O$. As the powder readily oxidizes if exposed to air, it must be preserved in tightly stoppered bottles.

The Pharmacopœia requires the presence of at least 15 per cent. of ferrous carbonate, determined by dissolving 1.16 Gm. of the powder in diluted sulphuric acid and titrating with potassium permanganate. Ferrous sulphate is formed and the subsequent reaction is identical with that already explained under that head. Each Cc. $\frac{N}{10}$ $KMnO_4$ solution, corresponding to 0.027742 Gm. $FeSO_4 + 10H_2O$, is also equivalent to 0.011573 Gm. $FeCO_3$; hence 15 Cc.

will be required to show 15 per cent. of 1.16 Gm., for 15 per cent. of 1.16 is 0.174 and $0.011573 \times 15 = 0.173585$.

FERROUS LACTATE. $Fe(C_3H_5O_3)_2 + 3H_2O$. This salt may be prepared by double decomposition between solutions of calcium lactate and ferrous sulphate, the newly formed calcium sulphate being completely removed by addition of alcohol; the filtrate is finally evaporated and crystallized. It may also be obtained by digesting pure iron wire with diluted lactic acid until reaction ceases, then filtering, concentrating, and crystallizing the solution. In the first process the reaction is as follows: $Ca(C_3H_5O_3)_2.5H_2O + FeSO_4.7H_2O = Fe(C_3H_5O_3)_2 + CaSO_4 + 12H_2O$; while, in the second process, ferrous lactate is formed with elimination of hydrogen; thus, $Fe_2 + 4HC_3H_5O_3 = 2Fe(C_3H_5O_3)_2 + H_4$.

Two varieties of ferrous lactate occur in commerce, one in well-defined crystalline crusts and another in the form of a crystalline powder. The first-named is to be preferred for pharmaceutical purposes and is the kind officially recognized; it is, as a rule, more soluble and less likely to have become oxidized. Ferrous lactate should be preserved in tightly stoppered bottles, in a dry place, as, upon exposure to moist air, it is gradually converted into a ferric salt.

The Pharmacopœia demands that ferrous lactate shall, after having been moistened with nitric acid, yield, upon ignition, not less than 27 nor more than 27.8 per cent. of an insoluble residue, consisting of ferric oxide only, which indicates a pure salt of the above composition, as 574.68 Gm. of crystallized ferrous lactate will yield 159.64 Gm. of ferric oxide, which is equivalent to 27.78 per cent.

SACCHARATED FERROUS IODIDE. The Pharmacopœia directs that this preparation shall be made by first preparing a solution of ferrous iodide, which is then evaporated, with the addition of sugar of milk, to dryness; finally some reduced iron is added and enough sugar of milk to bring the weight of the finished product to 100 Gm. for every 17 Gm. of iodine employed. The mixture is to be reduced to powder and carefully protected from air and light.

When iodine is brought together with an excess of iron, in the presence of a small quantity of water, the two elements combine with the development of heat, forming ferrous iodide, which dissolves the remainder of the iodine present and gradually the color of the solution changes to pale green, when all iodine has united with iron to form the compound FeI_2. Unless the concentrated solution be mixed with some sugar of milk before evaporation to dryness, the resulting product will be a deliquescent mass, difficult to remove from the capsule. Reduced iron, to the extent of 1 per cent. of the proposed weight of the finished product, is added to prevent, or at least retard, subsequent decomposition. The finished powder is very hygroscopic and by no means permanent, and there appears to be little or no advantage in this preparation over the syrup of ferrous

iodide, although it contains twice as much of the iron salt as the latter.

The valuation of saccharated ferrous iodide is made volumetrically by means of silver nitrate solution, silver iodide being precipitated and ferrous nitrate remaining in solution. In the official test, an unknown excess of the silver solution is added, which is determined by means of potassium sulphocyanate in the presence of nitric acid and ferric alum. The addition of nitric acid prevents the coloration of the liquid by the iron, and is always employed when silver nitrate is titrated by means of potassium sulphocyanate with ferric alum as an indicator.

In the official determination of ferrous iodide, both in the saccharated powder and the syrup of that name, several distinct reactions occur, namely:

1. All the iodine present is precipitated as silver iodide; thus, $FeI_2 + 2AgNO_3 = 2AgI + Fe(NO_3)_2$.

2. The excess of silver nitrate added is determined by precipitation as white silver sulphocyanate; thus, $AgNO_3 + KSCN = AgSCN + KNO_3$.

3. After all silver has been precipitated, the least further addition of potassium sulphocyanate solution produces a permanent reddish-brown tint, due to the reaction with ferric alum and consequent formation of ferric sulphocyanate; thus, $Fe_2(NH_4)_2(SO_4)_4 + 6KSCN = Fe_2(SCN)_6 + (NH_4)_2SO_4 + 3K_2SO_4$.

The first equation indicates that each Cc. of $\frac{N}{10}$ $AgNO_3$ solution represents 0.015477 Gm. of FeI_2; as the $\frac{N}{10}$ $AgNO_3$ and $\frac{N}{10}$ KSCN solutions exactly decompose each other, measure for measure, the number of Cc. of the latter necessary before a permanent brownish tint appears, subtracted from the number of Cc. of silver solution first added, leaves the number of Cc. of $\frac{N}{10}$ $AgNO_3$ solution actually used for precipitation of the iodine, which number multiplied by 0.015477 indicates the weight of ferrous iodide present in the sample. If 1.55 Gm. of saccharated ferrous iodide be used for the test, as directed, 20 Cc. (22-2) $\frac{N}{10}$ $AgNO_3$ solution will therefore be required to show 20 per cent of FeI_2, for 20 per cent. of 1.55 is 0.31 and $0.015477 \times 20 = 0.30954$.

Syrup of Ferrous Iodide. As already stated on page 224, this preparation is made by mixing a freshly prepared solution of ferrous iodide with simple syrup in such proportions that the mixture shall contain 10 per cent. by weight of the salt. In the preceding paragraph the preparation of solution of ferrous iodide has been explained. No attempt should be made to add the solution to the syrup until a pale-green color, entirely free from brown, has been acquired and all odor of iodine has been lost. The solution, heated to boiling, should be filtered rapidly in a covered funnel, the point of which dips below the surface of the syrup, in order to avoid contact with the air as far as possible.

Syrup of ferrous iodide is prone to decomposition if exposed to air, resulting in the oxidation of the ferrous into ferric salt, with gradual liberation of iodine. When thus changed, it can be restored to its original condition by exposing it to direct sunlight. The syrup should be preserved in small, completely filled, and tightly stoppered vials. Various additions have been suggested to prevent a change of the finished syrup, such as bright iron wire, glycerin, citric acid, etc., but the best results thus far have been obtained by the use of pure glucose in place of one-half of the simple syrup required; syrup thus prepared has been exposed in half-filled pint bottles to diffused daylight for several months, by G. H. Klie, of St. Louis, without undergoing any apparent change.

The valuation of syrup of ferrous iodide is conducted in exactly the same manner as given and explained under the preceding article. As the syrup contains only 10 per cent. of ferrous iodide, only one-half as much decinormal silver nitrate solution will be required as for a like weight of the saccharated powder.

Compound Iron Mixture. This preparation has already been considered on page 306 (which see). When freshly made, each cubic centimeter contains about 0.0025 Gm. of ferrous carbonate (about 1.14 grains in each fluidounce.

Ferric Ammonium Sulphate. $Fe_2(NH_4)_2(SO_4)_4+24H_2O$. This salt, resembling ordinary alum somewhat in chemical constitution, is obtained by dissolving ammonium sulphate in a boiling hot solution of ferric sulphate and setting the liquid aside to crystallize. If a slight addition of sulphuric acid be made to the solution, the crystals obtained will be more perfect in form and color.

The crystals are liable to deterioration by exposure to air and heat, hence they should be preserved in tightly stoppered bottles, in a cool place; when recently obtained or carefully preserved, they are of a beautiful pale-violet or hyacinthine color, but their solution in water is of a brownish-yellow color, gradually changing to red and depositing a basic salt.

Ferric ammonium sulphate, also known as ferric alum or ammonio-ferric alum, should contain not less than 11.6 per cent. of metallic iron in the form of ferric sulphate. The iron is determined volumetrically by the iodometric method, which has already been explained in connection with the valuation of reduced iron. The addition of hydrochloric acid, prescribed by the Pharmacopœia, is not essential for the reaction, but facilitates the same by converting the ferric sulphate into chloride, the latter salt decomposing potassium iodide more readily than the former. Since each Cc. of $\frac{N}{10}$ $Na_2S_2O_3$ solution represents 0.005588 Gm. of metallic iron, not less than 11.6 Cc. should be required to discharge the color of iodine completely in the official test, 0.56 Gm. of the salt being used; for 11.6 per cent. of 0.56 is 0.06496 and $11.6 \times 0.005588 = 0.064821$.

FERRIC CHLORIDE. $Fe_2Cl_6 + 12H_2O$. The official directions for preparing this salt consist in maceration of bright iron wire with about 3½ times its weight of hydrochloric acid, moderately diluted with water, oxidation of the resulting solution by means of nitric and hydrochloric acids and finally, after addition of a little more hydrochloric acid, evaporating the liquid to a definite weight and allowing it to crystallize.

The mixture of iron 15 Gm., hydrochloric acid 54 Gm. and water 25 Gm., is kept in a moderately warm place as long as effervescence continues, which is due to the escape of hydrogen, the ferrous chloride formed dissolving in the water; the equation, $Fe_2 + 4HCl = 2FeCl_2 + H_4$, illustrates the reaction. Not all the iron is dissolved, an excess being purposely directed in the Pharmacopœia to facilitate the reaction. The object of heating the liquid to the boiling-point before filtration and washing the flask and filter with hot water, is to insure complete solution of all ferrous chloride formed, as it sometimes crystallizes, owing to the density of the solution, especially in cold weather. The further addition of hydrochloric acid 28 Gm., should be made without delay, so as to avoid the formation and deposit of ferric oxychloride, since the ferrous chloride solution is readily oxidized by the air. The liquid, which has now assumed a deep green color, is poured slowly into a porcelain dish containing 8 Gm. of nitric acid, and then warmed. A change in color to reddish-brown at once occurs, owing to the conversion of the ferrous into ferric chloride, accompanied by effervescence and escape of red fumes, which may be illustrated by the following equation: $6FeCl_2 + 6HCl + 2HNO_3 = 3Fe_2Cl_6 + 2NO + 4H_2O$. The red fumes are due to nitrogen tetroxide, NO_2 or N_2O_4, resulting from a union of nitric oxide, NO, with some of the oxygen of the air.

It frequently happens that the color of the liquid remains blackish for some time; this is due either to a union of ferrous chloride with nitric oxide, in which case it disappears upon further heating as oxidation progresses, or, it may be, to an insufficiency of nitric acid and consequent imperfect oxidation.

To remove all nitrogen compounds, the liquid is heated on a sand-bath until free from nitrous odor, after which it is tested for ferrous salt, as prescribed, and, if more nitric acid is necessary, this should be added drop by drop to the hot liquid and only as long as effervescence results, as an excess of nitric acid is not readily removed. If ferrous salt is found absent, a test for nitric acid should be made and, if present, the liquid must be boiled on a sand-bath until entirely free therefrom; this is preferably done with careful addition of small quantities of hydrochloric acid, which facilitates the expulsion of nitric acid by decomposing it, and prevents the formation of oxychloride. Should the liquid, upon boiling to free it from nitric acid, separate a blackish-brown deposit on the sides or bottom of the dish, this would indicate ferric oxychloride, which can only be overcome by careful addition of hydrochloric acid to the hot liquid until a one-

per cent. solution of the latter in water remains clear upon boiling and cooling.

The final addition of 5 Gm. of hydrochloric acid to the liquid is for the purpose of preventing the formation of ferric oxychloride by having an excess of the acid present. Although the Pharmacopœia directs the addition of water, it is often found necessary, particularly if official acids have been used and the process carefully conducted, to evaporate the solution in order to obtain 60 Gm. of liquid. Experience has shown that better results are obtained if a solution containing 60 per cent. of anhydrous ferric chloride be set aside to absorb the requisite amount of water for crystallization than if it be evaporated to the crystallizing point. The theoretical yield of the official formula is about 65 Gm. (64.6) of the crystallized salt, provided hydrochloric acid of official strength has been employed.

Ferric chloride is a very deliquescent salt and, upon exposure to sunlight, is gradually reduced to ferrous chloride, hence it must be preserved in tightly stoppered bottles protected from light; corks coated with paraffin are preferable to glass stoppers.

The Pharmacopœia requires that 20 per cent. of metallic iron shall be represented in the salt, which is determined by the iodometric method already explained on page 488. The equation $(Fe_2Cl_6 + 12H_2O) + 2KI = I_2 + 2FeCl_2 + 2KCl$ shows that 539.5 parts of the official salt will liberate 253.06 parts of iodine and, as each Cc. $\frac{N}{10}$ $Na_2S_2O_3$ solution corresponds to 0.005588 Gm. of metallic iron, 20 Cc. should be required to decolorize the iodine liberated by 0.56 Gm. of crystallized ferric chloride of the above composition.

Ferric Citrate. This preparation is obtained by evaporating the official solution of ferric citrate to a syrupy consistence and then spreading the liquid on glass plates by means of a broad flat brush, and drying, in suitable drying-closets, at a moderate temperature, so that the salt will be obtained in perfect scales. A temperature exceeding 60° C. (140° F.) should not be employed, otherwise the salt will be slowly reduced to a ferrous compound. The usual yield is from 42 to 44 per cent. of the weight of solution evaporated, and failure to obtain perfect scales may be due to insufficient concentration of the liquid before spreading it on glass or too high a temperature in drying.

Although all scale salts of iron contain water of hydration, the amount present varies, not only for different salts, but also for different lots of the same salt, and is dependent upon the temperature employed in scaling, subsequent exposure, etc.; no definite formula expressing the composition of the scale salts of iron therefore can be given. Carefully prepared ferric citrate was found by F. B. Power to contain 31.9 per cent. of water, which would correspond very nearly to the formula, $Fe_2(C_6H_5O_7)_2 + 12H_2O$, while some commercial samples contained but 8.4 and 15.2 per cent. In estimating the water of hydration, a temperature of 100° C. (212° F.)

The Pharmacopœia, with the view of economizing time in cases of emergency, recommends that the dilute solution of ferric sulphate and the mixture of magnesia and water be always kept on hand, ready for immediate use. The former consists of 50 Cc. of the official solution of ferric sulphate and 100 Cc. of water; the latter, of 10 Gm. of calcined magnesia added to 750 Cc. of water.

FERRIC HYPOPHOSPHITE. This salt can be conveniently prepared by a method proposed by F. X. Moerk, in 1889, which consists in placing 30 Gm. of calcium hypophosphite in a flask with 100 Cc. of distilled water and adding gradually 49.5 Gm. of the official ferric chloride solution, shaking well after each addition. The mixture is allowed to stand for three days, with frequent agitation, then filtered and washed until all calcium has been removed. The yield by this method is large and the product fully up to the official requirements.

It was at one time suggested that ferric hypophosphite could be made by mixing solutions of calcium hypophosphite and ferrous sulphate, removing the precipitated calcium sulphate by filtration and evaporating the solution of ferrous hypophosphite to dryness. It was supposed that the ferrous salt was, by oxidation during the evaporation, converted into ferric hypophosphite; but, instead of the normal salt, a basic hypophosphite, $Fe_2O(PH_2O_2)_4$, is obtained, for want of a sufficiency of acid, as is similarly the case with the official solution of ferric subsulphate. Double decomposition of solutions of ferric sulphate or chloride and sodium hypophosphite is also impracticable, as the freshly precipitated ferric hypophosphite has been found quite soluble in water, thus considerable loss would be entailed during the necessary washing of the precipitate.

Ferric hypophosphite is sparingly soluble in water, but dissolves readily in a warm strong solution of an alkali citrate and, in this form, is used in the preparation of certain syrups.

The Pharmacopœia requires the official salt to contain 98.1 per cent. of absolute $Fe_2(PH_2O_2)_6$, which is determined volumetrically with potassium permanganate, as in the case of other hypophosphites. The following equation, $5Fe_2(PH_2O_2)_6 + 24KMnO_4 + 36H_2SO_4 = 5Fe_2(PO_4)_2 + 20H_3PO_4 + 12K_2SO_4 + 24MnSO_4 + 36H_2O$, shows that 2505.2 parts of ferric hypophosphite require 3784.08 parts of potassium permanganate for complete oxidation, hence each Cc. of $\frac{N}{10}$ $KMnO_4$ solution corresponds to 0.0020877 Gm. of $Fe_2(PH_2O_2)_6$. In the official test, 0.1 Gm. of the salt being used, 47 Cc. (50–3) will be required to show 98.1 per cent., for 98.1 per cent. of 0.1 is 0.0981 and $0.0020877 \times 47 = 0.0981219$.

FERRIC PHOSPHATE, SOLUBLE. The official phosphate of iron, which occurs in scale form and is soluble in water, must not be confounded with the insoluble commercial article of a similar name. The latter is a slate-colored powder of variable composition, consisting of a mixture of insoluble ferrous and ferric phosphates, obtained

by precipitation of a solution of ferrous sulphate by means of sodium phosphate and drying the resulting product.

Soluble ferric phosphate is made, according to the Pharmacopœia, by adding 11 parts of crystallized sodium phosphate to a solution of 10 parts of ferric citrate in twice its weight of water, evaporating the resulting green-colored solution, at a temperature not exceeding 60° C. (140° F.), to a syrupy consistence and spreading the same on glass plates, as in the case of ferric citrate. It is important that unefflorescent sodium phosphate be used, as officially directed, to avoid an excess of this salt, which would cause the scales to become opaque and white on standing. The salt should be preserved in tightly corked bottles, in a dark place, otherwise its color will gradually darken and its solubility be impaired.

The exact composition of this salt cannot be stated, as it may be a mixture of ferric phosphate and sodium citrate or possibly a mixture of four salts, ferric and sodium phosphates and ferric and sodium citrates, incomplete decomposition having taken place; hence the name, sodio-citro-phosphate of iron, is frequently applied to the preparation.

The Pharmacopœia requires that soluble ferric phosphate shall contain iron in combination corresponding to 12 per cent. of that metal.

FERRIC PYROPHOSPHATE, SOLUBLE. This preparation closely resembles the preceding compound, and is made in a similar manner, except that sodium pyrophosphate is used in place of the phosphate and that the sodium and iron salts are used in equal proportions. Prior to 1882 this preparation was made by precipitating a white ferric pyrophosphate, $Fe_4P_2O_9$, from a solution of ferric sulphate by means of sodium pyrophosphate, dissolving this precipitate in solution of sodium or ammonium citrate and concentrating and scaling the solution so obtained. The present official process yields a more satisfactory product.

The composition of soluble ferric pyrophosphate is as uncertain as that of the preceding scale salt, hence no definite formula as to its constitution can be given. Like the soluble ferric phosphate, it must be carefully protected against exposure to air and light. The two preparations are both of a green color, the phosphate bright green, the pyrophosphate apple-green, but may be readily distinguished from each other by boiling some of the salt with sodium hydroxide solution, filtering, acidulating the filtrate with hydrochloric acid and adding some magnesia test mixture (see U. S. Pharmacopœia) and a slight excess of ammonia water; in the case of the phosphate, a white crystalline precipitate of ammonium magnesium phosphate, NH_4MgPO_4, will occur, while the solution of the pyrophosphate will not be disturbed at all.

Although ferric pyrophosphate in scales is usually known in commerce simply as pyrophosphate of iron, it is best always to designate it as soluble pyrophosphate of iron, because the true ferric pyrophos-

phate also occurs on the market (although rarely), in the form of a white insoluble powder.

The amount of iron present in this preparation is required by the Pharmacopœia to be equivalent to 10 per cent. of metallic iron. The method of determination differs from that designated for the other scale salts of iron, in directing the addition of a much larger proportion of hydrochloric acid; this is done to insure complete solution and conversion into chloride of the true ferric pyrophosphate, which is precipitated on the first addition of the acid. The use of a larger amount of acid also demands the subsequent addition of more water, so as to avoid any risk of decomposition of the potassium iodide by the strong acid itself.

Ferric Valerianate. This salt is best obtained by double decomposition between cold solutions of ferric sulphate and sodium valerianate, washing the resulting precipitate with a little cold water and drying at a moderate temperature. The composition of ferric valerianate is variable, depending upon the care employed in washing the precipitate and the temperature at which it is dried. The normal salt would have the composition, $Fe_2(C_5H_9O_2)_6$, but the commercial product is often mixed with basic salt, as shown by its increased yield of ferric oxide upon ignition.

Ferric valerianate is rarely used in other than pill-form, although it is readily soluble in alcohol. Owing to the variable composition of the salt the Pharmacopœia allows a variation of 5 per cent. in the amount of metallic iron represented, requiring the same to be not less than 15 nor more than 20 per cent.

Iron and Ammonium Citrate. This preparation resembles the official ferric citrate, in appearance, but is far more readily soluble than it in cold water. It is obtained by mixing 10 volumes of solution of ferric citrate with 4 volumes of 10 per cent. ammonia water, concentrating and scaling the solution exactly as in the case of ferric citrate. The resulting product must of necessity be of variable composition, both as regards the amount of water of hydration and also the relative proportions of ferric and ammonium citrates present.

The official title, iron and ammonium citrate, would indicate a true double salt, which, when anhydrous, should be of uniform composition; such is not the case, however, and, as the Pharmacopœia requires the compound to contain exactly the same relative amount of iron as the plain ferric citrate, there cannot be much ammonium citrate present. The name soluble ferric citrate appears more appropriate and serves to distinguish it from the less soluble article. Inasmuch as ferric citrate is very rarely used in any other form than that of solution, it seems superfluous to have two preparations so nearly identical and differing from each other chiefly in degree of solubility.

Iron and ammonium citrate is more hygroscopic than ferric citrate, and, upon exposure to air, rapidly loses ammonia and becomes less soluble, hence it must be preserved in tightly stoppered bottles; light also has a deleterious effect upon it. If at any time the scale salt has suffered by age or careless exposure, ready solution can usually be effected by the cautious addition of a drop or two of ammonia water to the residue.

IRON AND AMMONIUM TARTRATE. In the official formula for the manufacture of this scale salt, the first step is the preparation of ferric hydroxide from 100 Cc. of solution of ferric sulphate, which has already been explained on page 496; the next step is to make a solution of acid ammonium tartrate by neutralizing a solution of 14.5 Gm. of tartaric acid exactly with ammonia water and adding to this another like weight of tartaric acid. The well-washed ferric hydroxide is then added in successive portions to the solution of acid ammonium tartrate and dissolved with the aid of a moderate heat, after which the solution is treated as in the case of the other scale salts of iron.

The reaction occurring may be illustrated by the following equation; $Fe_2(OH)_6+2NH_4HC_4H_4O_6=2NH_4(FeO)C_4H_4O_6+4H_2O$, in which the group FeO, to which the name ferryl has been given, acts as a univalent radical, like antimonyl. The scale compound, when carefully deprived of all water, probably has the composition expressed by the formula, $NH_4(FeO)C_4H_4O_6$.

Iron and ammonium tartrate is a deliquescent compound, requiring the careful exclusion of air and light. Like iron and ammonium citrate it is apt by age and exposure to become acid in character, and will then need the careful addition of a little ammonia water to restore neutrality and effect solution. It contains a larger proportion of iron than any other official scale salt, the Pharmacopœia requiring the equivalent of 17 per cent. of metallic iron.

IRON AND POTASSIUM TARTRATE. The official process for the preparation of this compound is very similar to that given for the preceding scale salt, except that acid potassium tartrate is used in place of acid ammonium tartrate. The hot solution of iron and potassium tartrate is not at once concentrated and spread on glass, but filtered and set aside for 24 hours to cool; during this time a precipitate separates and the liquid becomes acid. Upon carefully neutralizing with ammonia water a perfect solution is again produced, which is then concentrated and scaled.

Iron and potassium tartrate is recognized in the British Pharmacopœia under the name Ferrum Tartaratum, and is so prescribed in Great Britain. It occasionally happens that, as in the case of the preceding salt, it has become acid and difficultly soluble, probably owing to careless preservation; in such a case a few drops of ammonia water carefully added to the residue will restore perfect solubility.

The theoretical composition of the salt when anhydrous is $K(FeO)C_4H_4O_6$, based upon the equation, $Fe_2(OH)_6 + 2KHC_4H_4O_6 = 2K(FeO)C_4H_4O_6 + 4H_2O$. Like all the other scale salts of iron, it contains variable proportions of water. The Pharmacopœia requires the presence of an amount of iron in combination corresponding to 15 per cent. of metallic iron.

Iron and Quinine Citrate. The official scale compound of this name is unfamiliar to many pharmacists who have been in the habit of handling only the so-called soluble variety. It is prepared by dissolving 12 Gm. of dry quinine (pure alkaloid) in a strong solution of 85 Gm. of ferric citrate, with the aid of 3 Gm. of citric acid, concentrating the solution on a water-bath to a syrupy consistence, and finally scaling the same on plates of glass. The yield is intended to be 100 Gm.

The official iron and quinine citrate is intended chiefly to be used in the form of pills, tablets, etc., but not in solution; for, although it is completely soluble in water, it dissolves very slowly. It is of a reddish-brown color, somewhat resembling ferric citrate in appearance, and deliquesces slowly in damp air.

The Pharmacopœia demands that the scale salt shall contain not less than 11.5 per cent. of dried quinine and an amount of iron corresponding to 14.5 per cent. of that metal. Both can be determined in one sample, the quinine gravimetrically and the iron by the iodometric method, and thus much time and labor saved. The official estimation of the quinine is easily accomplished; the addition of ammonia water to a solution of the salt precipitates the quinine as alkaloid, which, dissolving readily in the chloroform, can be withdrawn and the treatment with chloroform repeated twice, so as to insure the complete removal of the alkaloid. A globular separator (see Fig. 138, page 145) is better adapted for the operation than one of cylindrical shape, as, by simple rotation, the two liquids are brought into sufficiently intimate contact for abstraction of the alkaloid by the chloroform, and separation takes place rapidly; if shaking must be resorted to, it frequently happens that an emulsion results, which requires considerable time for separation. Owing to the low boiling-point of chloroform (60° C. (140° F.)), the liquid should be evaporated with moderate heat only, so as to avoid loss by spurting, the residue being afterward dried at 100° C (212° F.) to constant weight.

The residuary aqueous liquid retains all the ferric citrate, and, if 25 Cc. of the same be used, after removal of all the chloroform and ammonia and dilution to 50 Cc., this will represent exactly one-half of the scale salt originally used, and therefore 14.5 Cc. of $\frac{N}{10}$ $Na_2S_2O_3$ solution will be necessary to indicate 14.5 per cent. of metallic iron, 1.12 Gm. having been used in the test. One-half of 1.12 is 0.56 and 14.5 per cent. of 0.56 is 0.0812; hence, as each Cc. of $\frac{N}{10}$ $Na_2S_2O_3$ solution represents 0.005588 Gm. of metallic iron, 14.5 Cc. will be equivalent to 0.081026 Gm.

SOLUBLE IRON AND QUININE CITRATE. As stated before, this is the salt generally dispensed by pharmacists, and is, in fact, the article usually sold by the jobber when citrate of iron and quinine is ordered. The Pharmacopœia has added the adjective "soluble" to the title of this salt to distinguish it from the less soluble reddish-brown variety; when the latter is wanted, pharmacists should always specify it by adding the letters U. S. P. to the name.

Soluble iron and quinine citrate differs in composition from the preceding salt only in containing ammonia, which is combined with citric acid, whereby the solubility of the compound is greatly increased, just as in the case of iron and ammonium citrate. The ammonia water is added to the solution of iron and quinine citrate first prepared as long as the precipitate formed is redissolved; an excess of ammonia must be carefully avoided. The solution acquires a greenish-yellow color and yields greenish, golden-yellow scales, which readily absorb moisture upon exposure to the air and are rapidly soluble in cold water.

The estimation of the iron and quinine is made exactly as in the plain iron and quinine citrate, the required proportion of each being identical in both salts.

IRON AND STRYCHNINE CITRATE. For the preparation of this compound the Pharmacopœia directs the use of iron and ammonium citrate, in order to obtain at once a readily soluble product; 1 Gm. each of strychnine and citric acid are dissolved in about 20 Cc. of water and added to a solution of 98 Gm. of iron and ammonium citrate in its own weight of water, the mixed liquids being concentrated and scaled on glass like other scale salts.

The Pharmacopœia requires for this preparation the presence of not less than 0.9 nor more than 1 per cent. of strychnine and a proportion of ferric citrate corresponding to 16 per cent. of metallic iron. The assay is made in the same manner as prescribed for iron and quinine citrate.

SOLUTION OF FERRIC ACETATE. An aqueous solution of ferric acetate, $Fe_2(C_2H_3O_2)_6$, containing about 31 per cent. of the anhydrous salt. The Pharmacopœia directs that it be prepared by dissolving well-washed ferric hydroxide in glacial acetic acid, and since the presence of even traces of ammonium salts has been found to interfere with the stability of the solution, the precipitated hydroxide is directed to be washed with boiling water until a reaction for ammonium compounds can no longer be obtained in the washings. This is an important part of the process, as experiments made with this preparation a few years ago demonstrated the fact that a solution made with ferric hydroxide absolutely free from ammonium and other alkali compounds remained clear, even when exposed to the heat of a boiling-water bath for some time, while solutions prepared with imperfectly washed ferric hydroxide began to deposit basic ferric acetate, even at a moderate elevation of temperature in a short time.

The complete removal of ammonium sulphate from ferric hydroxide with cold water is not readily accomplished, and although the treatment with boiling water renders the precipitate more compact, changing it to an oxyhydrate, there will be no difficulty in dissolving it in the glacial acetic acid.

The official solution of ferric acetate has a specific gravity of about 1.16, at 15° C. (59° F.), and contains, in each Cc., very nearly 0.36 Gm. of anhydrous ferric acetate, or about 164 grains in each fluidounce. The Pharmacopœia requires the solution to contain the equivalent of 7.5 per cent. of metallic iron, which is determined by the iodometric method, after conversion of the ferric acetate into ferric chloride, by means of hydrochloric acid.

Solution of Ferric Chloride. An aqueous solution of ferric chloride, Fe_2Cl_6, containing about 37.8 per cent. of the anhydrous salt. The preparation of this solution has already been fully explained under Ferric Chloride (see page 494); the two preparations are made exactly alike, except that in the case of dry ferric chloride the solution is evaporated to a certain weight and allowed to crystallize, while in the case of the official solution it is brought up to a certain density, by the addition of water, if necessary.

Solution of ferric chloride contains a small amount of free hydrochloric acid, but should be absolutely free from ferrous salt and ferric oxychloride, as well as nitric acid and other nitrogen compounds. Commercial solutions of ferric chloride are frequently contaminated with ferric oxychloride and nitrous odors are often perceptible.

The official solution has a specific gravity of about 1.387, at 15° C. (59° F.), and contains nearly 0.524 Gm. of anhydrous ferric chloride in each Cc., or about 240 grains in each fluidounce; its chief use in pharmacy is for the preparation of the tincture of ferric chloride. The Pharmacopœia requires that the solution shall contain an amount of ferric chloride corresponding to 13 per cent. of metallic iron, which is determined exactly as in the case of the dry salt.

Solution of Ferric Citrate. An aqueous solution of ferric citrate containing about 32.85 per cent. of the anhydrous salt, $Fe_2(C_6H_5O_7)_2$, which corresponds to 7.5 per cent. of metallic iron, together with a slight excess of citric acid. This solution is prepared in a very similar manner to solution of ferric acetate, except that citric acid is used in place of glacial acetic acid and that the precipitate of ferric hydroxide is washed with cold, instead of hot, water.

The equation, $2(H_3C_6H_5O_7 + H_2O) + Fe_2(OH)_6 = Fe_2(C_6H_5O_7)_2 + 8H_2O$, shows that 419 parts of citric acid require 213.52 parts of ferric hydroxide to form 488.84 parts of the normal citrate. In the official formula for this solution, 1050 Gm. of solution of ferric sulphate are used, which theoretically will yield 161.18 Gm. of ferric hydroxide, but there is always some loss in washing and transferring the precipitate, so that the amount of citric acid prescribed, 300 Gm.,

is usually in slight excess; 300 Gm. of citric acid require 152.87 Gm. of ferric hydroxide, and the amount of free acid in the finished solution will depend upon the care with which the loss of hydroxide is controlled.

The official solution of ferric citrate has a specific gravity of about 1.250, at 15° C. (59° F.). The amount of iron salt required by the Pharmacopœia corresponds to 7.5 per cent. of metallic iron, which is determined as in the case of solution of ferric acetate.

SOLUTION OF FERRIC NITRATE. An aqueous solution of ferric nitrate, $Fe_2(NO_3)_6$, containing about 6.2 per cent. of the anhydrous salt. This is the weakest of the official simple iron solutions and is prepared by dissolving freshly precipitated ferric hydroxide in nitric acid.

The nitric acid used should be of full official strength, in order to produce a normal ferric nitrate, for which the prescribed quantity of acid is sufficient; 180 Gm. of solution of ferric sulphate will yield 27.63 Gm. of ferric hydroxide, which require 48.82 Gm. of absolute, or 71 Gm. of official, nitric acid, as shown by the equation, $Fe_2(OH)_6 + 6HNO_3 = Fe_2(NO_3)_6 + 6H_2O$. If a weaker acid be employed, basic ferric nitrates of deeper color will be produced. The Pharmacopœia requires that the solution shall contain an amount of ferric nitrate corresponding to 1.4 per cent. of metallic iron, which is estimated as in the case of ferric acetate solution.

Solution of ferric nitrate has a specific gravity of about 1.050 at 15° C. (59° F.) and contains in each Cc. about 0.065 Gm., or in each fluidounce about 30 grains, of the anhydrous salt.

SOLUTION OF FERRIC SUBSULPHATE. An aqueous solution of basic ferric sulphate of variable composition. It is prepared by adding 675 Gm. of ferrous sulphate to a heated mixture of 65 Gm. each of sulphuric and nitric acids and 500 Cc. of water; when effervescence ceases, the liquid is tested for ferrous salt, and, if this be found present, nitric acid is added, drop by drop, to the hot liquid, as long as it causes further effervescence and the disengagement of red fumes. Finally the liquid is boiled until a clear ruby-red solution is obtained, entirely free from nitrous odor, and is diluted with water to the weight of 1000 Gm.

The ferrous sulphate is used in the form of a coarse powder and added to the hot acid mixture in divided portions, in order to avoid a violent reaction. In the presence of nitric and sulphuric acids, oxidation takes place, converting the ferrous into a ferric salt, but, owing to an insufficient amount of sulphuric acid, a basic, instead of a normal, ferric sulphate is produced, the composition of which is variable, hence no definite formula can be assigned to it, although the following, $Fe_4O(SO_4)_5$, is used by some to illustrate the nature of the salt. In the preparation of this, as well as the next following solution, copious red vapors are evolved, due to the escape of nitric

oxide into the air, and the liquid assumes a black tint temporarily, on account of a union between the ferrous sulphate and nitric oxide; these phenomena have already been explained in connection with the manufacture of ferric chloride.

If a little sulphuric acid be added to solution of ferric subsulphate, the color becomes lighter, and, if added to the extent of one-half the volume of the latter, a white mass, consisting of anhydrous ferric sulphate, will separate.

The name Monsel's Solution is usually applied to this preparation, which is also prescribed by physicians as solution of persulphate of iron; although chemically incorrect, this last name is frequently employed in this country, when the official solution of the subsulphate is intended, particularly by some of the older physicians.

Solution of ferric subsulphate is a dense solution, having a specific gravity of about 1.550, at 15° C. (59° F.), and is apt to separate a semi-solid crystalline whitish mass upon standing, particularly in the cold. This is not a sign of deterioration, but is due to the concentration of the solution, and can be overcome by placing the bottle in warm water for a while and agitating, when perfect solution will be restored. The Pharmacopœia demands that the amount of basic ferric sulphate present in this solution shall correspond to 13.6 per cent. of metallic iron, to be estimated in the same manner as indicated for the other iron solutions.

Solution of Ferric Sulphate. An aqueous solution of normal ferric sulphate, $Fe_2(SO_4)_3$, containing about 28.7 per cent. of the salt. This solution is not used medicinally, being only employed for the preparation of other iron compounds. It is made in the same manner as solution of ferric subsulphate, except that a larger proportion of acids is used, a different product being, therefore, obtained. The following equation, $6(FeSO_4 + 7H_2O) + 3H_2SO_4 + 2HNO_3 = 3Fe_2(SO_4)_3 + 2NO + 46H_2O$, shows that the reaction results in the formation of a normal salt, which is the only point of difference in the composition of this and the preceding solution.

Solution of ferric sulphate is known in the British Pharmacopœia as Solution of Persulphate of Iron, but the official Latin title of the United States Pharmacopœia, Liquor Ferri Tersulphatis, is preferable, as at once indicating the true nature of the chemical compound present. It can be readily distinguished from Monsel's solution by a lower density and lighter color, and also by not separating white ferric sulphate upon addition of one-half its volume of sulphuric acid. The solution has a specific gravity of about 1.320, at 15° C. (59° F.), and is required to contain an amount of ferric sulphate corresponding to 8 per cent. of metallic iron.

Solution of Iron and Ammonium Acetate. This well-known preparation is usually prescribed by physicians as "Basham's Mixture," or under its old official (1880 Pharmacopœia) title, Mistura

Ferri et Ammonii Acetatis. It is readily prepared by adding to 200 Cc. of solution of ammonium acetate successively, 30 Cc. of diluted acetic acid, 20 Cc. of tincture of ferric chloride, 100 Cc. of aromatic elixir, 100 Cc. of glycerin, and sufficient water to bring the total volume up to 1000 Cc.

As its name indicates, the solution contains both iron and ammonium acetates, the former salt, to which the deep red color of the liquid is due, being formed, at the time of preparation, by mutual decomposition between the ferric chloride and a part of the ammonium acetate; a small amount of ammonium chloride is also formed. It is important that the solution of ammonium acetate be not alkaline, so that, upon addition of the diluted acetic acid, an excess of the latter shall be present, to avoid the formation of basic ferric acetate when the tincture of ferric chloride is added.

Although the Pharmacopœia directs that this preparation should be freshly made when wanted, this is not necessary, as, when prepared strictly according to the present official formula, it keeps well for months, without showing any signs of change, even in diffused light or during hot summer weather. The old formula of 1880 was defective, but the use of glycerin, in place of syrup, has completely remedied the evil.

Tincture of Ferric Chloride. This is a hydro-alcoholic solution of ferric chloride, containing about 13.6 per cent. of the anhydrous salt. The Pharmacopœia directs that 250 Cc. of solution of ferric chloride shall be mixed with sufficient alcohol to yield 1000 Cc.; this will require slightly more than 750 Cc. of alcohol, on account of the contraction of volume which invariably results when aqueous liquids and alcohol are mixed. The official directions, to set the mixture aside for a period of three months, are for the purpose of allowing certain changes to take place before dispensing the tincture; these changes are due to reaction between the acid solution of ferric chloride and alcohol, resulting in the formation of ethyl chloride and other ethereal products, which modify the odor of the preparation to some extent, and are said also to possess marked medicinal properties. By some authorities, it is claimed that these changes will not be completed at the end of three months, and that, in fact, they will continue for a period of six or nine months.

Occasionally the mixture is found to deposit a yellowish-brown sediment; this is due to ferric oxychloride, and is an evidence that the solution of ferric chloride used was deficient in hydrochloric acid, and, therefore, not properly made.

Tincture of ferric chloride contains, in each Cc., about 0.130 Gm. of anhydrous, or 0.216 Gm. of official, ferric chloride, equivalent to about 60 and 100 grains respectively in each fluidounce. Upon exposure to sunlight, it is gradually changed in color, assuming a greenish-brown tint, owing to reduction of the ferric to ferrous salt, hence it should be protected from strong light.

The proportion of ferric chloride present in the official tincture corresponds to 4.7 per cent. of metallic iron and is determined, in the usual manner, with potassium iodide and sodium thiosulphate.

Besides the official preparations of iron, the following are employed:

ALBUMINATE OF IRON. This compound occurs in the form of yellowish-brown scales, obtained by concentrating an alkaline solution of ferric albuminate (see solution of albuminate of iron), with the aid of a low heat, spreading the same on plates of glass and drying at a moderate temperature. It represents between 3 and 4 per cent. of metallic iron and must be carefully preserved.

ARSENATE OF IRON. This preparation, as found in the market, is of variable composition. It is recognized in the British Pharmacopœia as arseniate of iron and directed to be made by mixing a solution of sodium arsenate with one of ferrous sulphate and adding some sodium bicarbonate. Ferrous arsenate, $Fe_3As_2O_8$, is precipitated, which is well washed and dried, in the meantime undergoing oxidation and changing from greenish-white to olive-green or bluish-green in color.

BENZOATE OF IRON. Ferric Benzoate, $Fe_2(C_7H_5O_2)_6$. This salt may be obtained as a pale-brownish powder by adding a concentrated solution of sodium benzoate to a solution of ferric sulphate, washing the resulting precipitate with a little cold water and drying the same.

BROMIDE OF IRON. Ferrous Bromide, $FeBr_2$. This compound is prepared by direct union of iron and bromine in the presence of water; an excess of iron wire is used, and, when a pale-green solution results, it is filtered and evaporated to dryness in a bright iron dish. It forms a dark, almost black mass, which turns brown through oxidation upon exposure to air, hence it must be preserved in tightly stoppered bottles.

DIALYZED IRON. Under this name, a solution of a highly basic ferric oxychloride has been used by physicians for many years. It is recognized in the British and German Pharmacopœias. The official German preparation is obtained by simply dissolving freshly prepared ferric hydroxide in water, with the aid of a very small quantity of hydrochloric acid and a gentle heat, but is not dialyzed subsequently. The British Pharmacopœia directs a process which is about the same as that usually followed in this country, namely, a solution of ferric chloride is saturated with freshly made ferric hydroxide, the liquid placed in a dialyzer (see page 152) and suspended in water, which is frequently renewed, as long as the latter shows

any reaction for chlorides. Complete removal of ferric chloride is neither practicable nor desirable, and highly basic oxychlorides give no reaction with silver nitrate. The solution of ferric oxychloride remaining in the dialyzer is then diluted with sufficient water so that 100 parts by weight, when evaporated and dried at a temperature not above 100° C. (212° F.), shall yield 5 parts of solid residue. The composition of the ferric oxychloride found in commercial dialyzed iron varies, ranging between $Fe_2Cl_6 + 10F_2O_3$, and $Fe_2Cl_6 + 35Fe_2O_3$; still more highly basic oxychlorides can be obtained by dialysis, but the solutions are apt to gelatinize on standing.

FERROCYANIDE OF IRON. Ferric Ferrocyanide, $Fe_4(Fe(CN)_6)_3$. When a solution of potassium ferrocyanide is gradually added to a dilute solution of ferric sulphate, a dark blue precipitate, having the above composition, is obtained. The precipitate must be well washed with boiling water to remove all potassium sulphate and is then dried.

IODIDE OF IRON. Ferrous Iodide, FeI_2. This preparation is obtained by first making a solution of ferrous iodide, as already explained in connection with saccharated iodide of iron, and evaporating this, in a bright iron dish, to dryness. It occurs as a very deliquescent black mass, which must be carefully preserved in tightly stoppered bottles.

MALATE OF IRON. Impure ferrous malate occurs in the form of a blackish-green mass, obtained by digesting the juice of sour apples with iron filings, filtering and evaporating the solution to the consistence of an extract. It is recognized in the German Pharmacopœia under the name of Extractum Ferri Pomatum.

OXALATE OF IRON. Ferrous Oxalate, FeC_2O_4. This salt may be conveniently prepared by mixing a solution of acid ammonium oxalate with one of ferrous sulphate; the lemon-yellow precipitate of ferrous oxalate is well washed with water until a reaction for sulphuric acid is no longer obtained, and then dried. This process affords a better yield than if ferrous sulphate be treated with pure oxalic acid, since some of the salt would be lost by solution in the diluted sulphuric acid.

PHOSPHATE OF IRON. This compound has already been mentioned in connection with the soluble salt of the same name. It is a variable mixture of ferrous and ferric phosphates with ferric oxide and is recognized in the British Pharmacopœia, which directs it to be prepared by adding a solution of sodium phosphate to one of ferrous sulphate, finally adding some sodium bicarbonate. The precipitate of ferrous phosphate, $Fe_3(PO_4)_2$, is washed and dried, during which time it is slowly oxidized. Phosphate of iron is a slate-blue amorphous powder, insoluble in water.

PEPTONATE OF IRON. If egg-albumen be digested with pepsin and very dilute hydrochloric acid, for some time, at a temperature not exceeding 40° C. (104° F.), a solution of peptone will be obtained, which, after being neutralized with solution of soda and added to a solution of ferric oxychloride, yields a precipitate of ferric peptonate. In order to obtain the compound in soluble form the precipitate is dissolved in water, with the aid of a little hydrochloric acid and heat, the solution evaporated to a syrupy consistence and spread on plates of glass to be dried at a temperature not above 30° C. (86° F.).

SACCHARATED OXIDE OF IRON. This preparation, known also as soluble oxide of iron, is officially recognized in the German Pharmacopœia and used to some extent in this country. It is prepared by adding to freshly prepared ferric hydroxide a given proportion of sodium hydroxide solution and sugar, heating the mixture to perfect solution, then evaporating to dryness, powdering and incorporating with it sufficient sugar to bring the product up to a definite weight, representing the equivalent of 3 per cent. of metallic iron. The exact composition of the reddish-brown powder, is as yet not clearly understood; it is considered to be a sodio-ferric saccharate, the presence of the alkali being essential, as, with sugar alone, ferric hydroxide does not form a perfectly soluble compound.

SALICYLATE OF IRON. Ferrous Salicylate. $Fe(C_7H_5O_3)_2$. This is best prepared by dissolving freshly precipitated ferrous carbonate in water, by means of salicylic acid, with the aid of a gentle heat, filtering and evaporating the solution to dryness on a water-bath.

SOLUTION OF ALBUMINATE OF IRON. An aromatic, alkaline solution of ferric albuminate prepared, according to the German Pharmacopœia, as follows: A solution of 35 parts of dry egg-albumen in 1000 parts of water is slowly added to a mixture of 120 parts of solution of oxychloride of iron and 1000 parts of water, the resulting precipitate is well washed with water until all chlorine has been removed and then dissolved in 3 parts of solution of soda (sp. grav. 1.17) diluted with 50 parts of water. To this solution are added 150 parts of alcohol, 100 parts of cinnamon water, 2 parts of aromatic tincture, and sufficient water to bring the total weight up to 1000 parts. It represents about 0.4 per cent. of metallic iron.

SUBCARBONATE OF IRON. Under this name an amorphous reddish-brown powder has long been known in pharmacy and was, at one time, recognized in the Pharmacopœia (1870). It is a variable mixture, the composition depending upon age and the temperature at which it has been dried, and consists chiefly of ferric oxide and hydroxide with some ferrous carbonate. The manner of preparing it is to mix solutions of ferrous sulphate and sodium carbonate together, whereby greenish-white ferrous carbonate is precipitated; this is

thoroughly washed with water and dried, during which operation it rapidly darkens and becomes oxidized with the elimination of carbon dioxide. Subcarbonate of iron is practically identical with ferric oxyhydrate $Fe_2O_3+Fe_2(OH)_6$, and is often designated as red steel-dust by the public.

Syrup of Arsenate of Iron. A preparation of the National Formulary containing about $\frac{1}{60}$ grain of ferric arsenate, Fe_2AsO_4, in each fluidounce. It is made by preparing a solution of ferric arsenate from sodium arsenate and ferric citrate and mixing this with simple syrup, the ferric arsenate being held in solution by the newly formed sodium citrate.

Syrup of Citro-iodide of Iron. This preparation also known as "tasteless syrup of iodide of iron" is made according to the National Formulary by dissolving iodine in a solution of ferrous iodide and adding this solution to a solution of potassium citrate; as soon as a deep-green color has developed, sugar is added and dissolved by agitation. Each fluidounce contains about 29 grains of ferric iodide, Fe_2I_6, equivalent to about 0.0635 Gm. in each Cc.

Syrup of Soluble Oxide of Iron. This syrup may be conveniently prepared extemporaneously as wanted, by forming a solution of equal parts by weight of saccharated oxide of iron, water, and simple syrup. This is the formula given by the German Pharmacopœia; a more tedious process for making the syrup from solution of ferric chloride is given in the National Formulary. Each fluidounce of the syrup represents about $6\frac{1}{2}$ grains of metallic iron or about 0.0143 Gm. in each Cc.

Tincture of Citro-chloride of Iron. The National Formulary directs this preparation, which is better known as "tasteless tincture of iron," to be made by adding sodium citrate to a diluted solution of ferric chloride and heating until perfect solution is effected. Alcohol is then added and finally sufficient water to make up the required volume. The tincture is of a deep-green color and the amount of iron represented is about the same as in the official tincture of ferric chloride.

CHAPTER XLVIII.

THE COMPOUNDS OF MANGANESE AND CHROMIUM.

Of these two metals the Pharmacopœia recognizes but three compounds, and even these are not frequently employed. The official preparations are as follows:

Official English Name.	Official Latin Name.
Manganese Dioxide,	Mangani Dioxidum.
Manganese Sulphate,	Mangani Sulphas.
Chromic Acid,	Acidum Chromicum.

Manganese Dioxide. MnO_2. The Pharmacopœia recognizes native crude manganese dioxide, commonly known as pyrolusite, which, while suitable for the manufacture of chlorine and similar purposes, is frequently unfit for internal use, owing to the large proportion of foreign matters present. The quality of commercial manganese dioxide is, of course, very variable, some very rich specimens having occasionally been encountered. An artificial product occurs in the market, in the form of a very dark, almost black, tolerably fine powder, which is far superior to the crude article, and should alone be used for dispensing purposes. It is possibly prepared by gentle ignition of manganese nitrate or by moderate heating of manganese hydroxide.

The Pharmacopœia admits manganese dioxide containing only 66 per cent. of pure MnO_2, but the artificial article put on the market by manufacturing chemists is usually guaranteed to represent 90 per cent. and over. The valuation is made by means of treatment with ferrous sulphate and hydrochloric acid, whereby all ferrous salt is converted into ferric salt, according to the following equation—$3MnO_2+12HCl+6(FeSO_4+7H_2O)=2Fe_2(SO_4)_3+Fe_2Cl_6+3MnCl_2+48H_2O$—showing that each molecule (or 86.72 parts) of pure manganese dioxide is capable of oxidizing two molecules (or 554.84 parts) of crystallized ferrous sulphate, or, in other words, 1 Gm. of MnO_2 will suffice for the complete oxidation of 6.398 Gm. of $FeSO_4+7H_2O$.

In the official test, 1 Gm. of the commercial article will convert the 4.22 Gm. of ferrous sulphate completely into ferric sulphate and chloride, so that the subsequent addition of potassium ferricyanide no longer causes a blue coloration, only, if at least 66 per cent. of pure MnO_2 be present, for 66 per cent. of 1 is 0.66 and 1 : 0.66 :: 6.398 : 4.22.

MANGANESE SULPHATE. Manganous Sulphate. $MnSO_4+4H_2O$. This salt is obtained by heating a mixture of manganese dioxide and sulphuric acid to dull redness, in a crucible, for some time; when cool, the mass is treated with water and filtered. The solution, if iron be present, is digested with manganous carbonate, filtered, concentrated and crystallized at a temperature not below 20° C. (68° F.). If the solution be allowed to crystallize at a temperature approaching 5° C. (41° F.), a salt will be obtained containing 7 molecules, or nearly 46 per cent. of water, while the official salt should contain only 4 molecules, or 32.29 per cent.

Manganous sulphate is used for the preparation of other manganese salts by mutual decomposition, such as the carbonate, hypophosphite, and iodide, which are occasionally used in pharmacy.

CHROMIC ACID. Chromic Trioxide. CrO_3. Although this compound is commercially designated as an acid, and is also recognized in the Pharmacopœia by that name, it is, strictly speaking, simply an anhydride and the name chromic trioxide or anhydride appears more appropriate.

It is prepared by adding sulphuric acid to a saturated solution of potassium dichromate, when the following reaction occurs: $K_2Cr_2O_7+2H_2SO_4=2CrO_3+2KHSO_4+H_2O$; the mixture becomes heated and, upon cooling, separates needle-shaped crystals of chromic anhydride, which are drained and dried on porous tiles. In order to remove the sulphuric acid generally adhering to the crystals, these are washed with small quantities of strong nitric acid and finally heated, in a porcelain dish, on a sand-bath, until nitrous odors are no longer perceptible.

The color of commercial chromic anhydride, is not uniform, depending upon the purity of the article; a light scarlet-red color usually indicates the presence of sulphuric acid, and such a product is, as a rule, very deliquescent. The Pharmacopœia demands the entire absence of sulphuric acid; such an article is of a deep purplish-red color and not very hygroscopic. Owing to its ready decomposition by organic substances, often with explosive violence, chromic anhydride should never be brought into contact with alcohol or glycerin, and should always be weighed on watch-glasses, never on paper; if its aqueous solution requires filtration, this must be done by means of asbestos or glass-wool.

CHAPTER XLIX.

THE COMPOUNDS OF MERCURY.

NEXT to the preparations of iron, those of mercury are the most important obtained from the heavy metals. Like the iron compounds, they are divided into two series, designated as mercurous and mercuric compounds respectively. In mercurous compounds, mercury appears univalent, while in mercuric compounds it acts like a bivalent element. The Pharmacopœia recognizes metallic mercury and twenty preparations of it and its compounds, as shown by the following list:

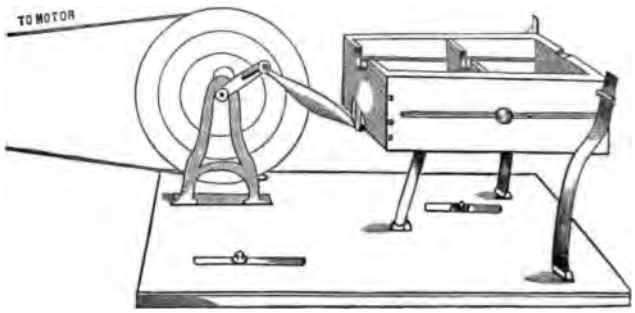
Official English Name.	Official Latin Name.
Mercury,	Hydrargyrum.
Mercury with Chalk,	Hydrargyrum cum Creta.
Ammoniated Mercury,	Hydrargyrum Ammoniatum.
Mild Mercurous Chloride,	Hydrargyri Chloridum Mite.
Yellow Mercurous Iodide,	Hydrargyri Iodidum Flavum.
Corrosive Mercuric Chloride,	Hydrargyri Chloridum Corrosivum.
Mercuric Cyanide,	Hydrargyri Cyanidum.
Red Mercuric Iodide,	Hydrargyri Iodidum Rubrum.
Yellow Mercuric Oxide,	Hydrargyri Oxidum Flavum.
Red Mercuric Oxide,	Hydrargyri Oxidum Rubrum.
Yellow Mercuric Subsulphate,	Hydrargyri Subsulphas Flavus.
Mass of Mercury,	Massa Hydrargyri.
Mercurial Ointment,	Unguentum Hydrargyri.
Mercurial Plaster,	Emplastrum Hydrargyri.
Ointment of Ammoniated Mercury,	Unguentum Hydrargyri Ammoniati.
Ointment of Mercuric Nitrate,	Unguentum Hydrargyri Nitratis.
Ointment of Yellow Mercuric Oxide,	Unguentum Hydrargyri Oxidi Flavi.
Ointment of Red Mercuric Oxide,	Unguentum Hydrargyri Oxidi Rubri.
Mercuric Oleate,	Oleatum Hydrargyri.
Solution of Mercuric Nitrate,	Liquor Hydrargyri Nitratis.
Ammoniac Plaster with Mercury,	Emplastrum Ammoniaci cum Hydrargyro.

MERCURY. Hg. Nearly all the commercial mercury is obtained by roasting the ore known as cinnabar, crude native sulphide of mercury, the sulphur escaping as sulphur dioxide, while metallic mercury is condensed and collected in suitable apparatus. As thus obtained, it is usually contaminated with lead, copper, and other metals, from which it is freed by treatment with diluted nitric acid; it is finally washed with water and dried. On a small scale mercury may be conveniently purified by shaking with solution of ferric chloride and subsequently washing with water. For medicinal purposes, only pure redistilled mercury, which possesses a bright lustre, should be used; if contaminated with dust and other mechanical impurities, mercury may be conveniently strained through a piece of close muslin or

chamois skin. For weighing small quantities of mercury, it is most conveniently transferred from the stock bottle to the balance by means of a drop-tube or pipette, as, owing to its great cohesiveness, it cannot be readily poured from a bottle.

MERCURY WITH CHALK. Although not so much used as formerly, this preparation, also known as "Gray Powder," is still a very important one, as it represents mercury in a fine state of division in powder-form, and is frequently used in infantile disorders. The official method of preparation depends upon extinguishment of the mercury by means of succussion, 38 Gm. of mercury being shaken with 10 Gm. of clarified honey, for 6 hours or longer in a strong bottle; this is best effected in a mechanical shaker, such as is shown in Fig. 279, which can be readily attached to a water motor connected

FIG. 279.



Mechanical shaker.

with a hydrant. The mixture of mercury and honey is afterward added to a thick, creamy paste, made of 57 Gm. of prepared chalk and a sufficient quantity of water, the whole being triturated until a uniform mixture results, which is finally dried at the ordinary temperature, and should be reduced to powder without trituration.

In this fine state of division, mercury is very prone to oxidation if exposed to air and light; hence the powder should be kept well protected from both. While traces of mercurous oxide cannot be entirely avoided, the presence of mercuric oxide should be carefully guarded against, and any change in color from gray to pink or reddish, indicating dangerous oxidation, would render the article unfit for use; neither should mercury with chalk be dispensed if the color has turned very dark-gray or blackish, as this shows excessive mercurous oxidation. In the official test, mercurous oxide is detected by precipitation, as calomel by hydrochloric acid, while the mercuric oxide is converted into mercuric chloride and is then precipitated either as mercuric sulphide, by hydrogen sulphide, or as calomel (being afterward reduced to metallic mercury) by stannous chloride

AMMONIATED MERCURY. NH_2HgCl. This compound, better known as white precipitate, is prepared by pouring a solution of mercuric chloride slowly, with constant stirring, into ammonia water, when the following reaction occurs: $HgCl_2 + 2NH_4OH = NH_2HgCl + NH_4Cl + 2H_2O$. The Pharmacopœia directs a solution of 100 Gm. of mercuric chloride in 2000 Cc. of distilled water, which, after filtration to remove any calomel present, is added to 150 Cc. of 10 per cent. ammonia water; both liquids are used cold, and the resulting precipitate is washed with 400 Cc. of cold water to which 20 Cc. of ammonia water have been added. Finally, the precipitate is dried, in a dark place, at a temperature not exceeding 30° C. (86° F.). These specific directions are for the purpose of avoiding the formation of a basic yellow compound, $NH_2(Hg_2O)Cl$, which is apt to occur by exposure to light or heat, and even excessive washing with plain water.

The constitution of ammoniated mercury may be explained in two different ways. The simplest view is to consider it as mercuric chloride, in which an atom of chlorine has been replaced by the group NH_2 (or amide), and, in that case, the name mercuric chloramide will be appropriate; the other view is that evidently taken by the Pharmacopœia in applying the synonym mercuric ammonium chloride to the compound, according to which, it is looked upon as ammonium chloride in which two atoms of hydrogen have been replaced by an atom of bivalent mercury.

Ammoniated mercury is also known as amido-chloride of mercury, and is sometimes prescribed by German physicians as hydrargyrum amidato-bichloratum.

MILD MERCUROUS CHLORIDE. Hg_2Cl_2. This well-known salt, commonly called calomel, is prepared by subliming a mixture of mercurous sulphate and sodium chloride in proper proportions. In order to obtain the product in the form of a soft fine powder, the vapors are conducted into a spacious chamber, into which steam is introduced simultaneously; the presence of aqueous vapor also frees the sublimate from mercuric chloride, some of which is always formed, by solution in the condensed water. Thus obtained, the product is known as hydrosublimed calomel. When mercurous chloride is sublimed without steam it becomes necessary to reduce the crystalline sublimate to fine powder, and wash it thoroughly with water until the washings are no longer affected by ammonia water or ammonium sulphide, showing the complete removal of mercuric chloride.

The mercurous sulphate used in the above process is made by moistening mercuric sulphate with water, adding an equivalent amount of mercury (200 parts for 296 parts of mercuric sulphate), and triturating the mixture until all globules of mercury disappear. The reaction between mercurous sulphate and sodium chloride, when heated together, is shown by the following equation: $Hg_2SO_4 + 2\,NaCl = Hg_2Cl_2 + Na_2SO_4$.

The appearance of calomel depends largely upon the degree of mechanical division: while usually white, the finer the powder the more yellowish the tint. When exposed to light it gradually undergoes decomposition and assumes a grayish color, mercuric chloride being formed, with the elimination of mercury.

Calomel has sometimes been prescribed by continental physicians under the names "aquila alba" and "mercurius dulcis."

YELLOW MERCUROUS IODIDE. Hg_2I_2. The official process for the preparation of mercurous iodide involves two distinct steps. First, mercurous nitrate is made by treating 50 Gm. of mercury with a mixture of 20 Cc. each of nitric acid and water, in a dark place, until reaction ceases and a little mercury remains undissolved: the salt separates in the form of crystals having the composition $Hg_2(NO_3)_2 + 2H_2O$, which are drained and dried on paper in the dark. 40 Gm. of the crystallized mercurous nitrate are then dissolved in 1000 Cc. of distilled water acidulated with 10 Cc. of nitric acid, and to this solution is added, slowly and with constant stirring, a solution of 24 Gm. of potassium iodide in 1000 Cc. of water, when the following reaction occurs: $(Hg_2(NO_3)_2 + 2H_2O) + 2KI = Hg_2I_2 + 2KNO_3 + 2H_2O$. The precipitate is drained on a filter and washed, first with water to remove all potassium nitrate and free acid, and afterward with alcohol, until the washings cease to be affected by hydrogen sulphide, to free it from mercuric iodide; lastly, it is dried in the dark, on paper, at a temperature not exceeding 40° C. (104° F.).

The addition of nitric acid is made to prevent the formation of a basic compound, which might otherwise occur; it is also important that the potassium iodide be added to the mercurous nitrate lest, by a reversal of the process, mercuric salt be formed, which enters into solution as potassium mercuric iodide, while mercury is precipitated, a reaction well known to occur between alkali iodides and mercurous iodide, and illustrated by the equation, $Hg_2I_2 + 2KI = (HgI_2 + 2KI) + Hg$.

Mercurous iodide must be carefully protected from light, as it readily undergoes decomposition. The true color of the salt, when pure, is bright yellow, hence all preparations of a green, or greenish-yellow color, must be looked upon as impure, the latter colors being due to an admixture of metallic mercury, which, in a finely divided state, is blue, and consequently causes a greenish mixture with the pure yellow salt.

Much green iodide of mercury is still sold by manufacturers, having been recognized in the Pharmacopœias of 1870 and 1880, but its production is due to a faulty process of preparation. When mercury and iodine, or mercury and mercuric iodide, are triturated together, yellow mercurous iodide is formed with variable proportions of mercuric iodide, some of the mercury remaining uncombined in a finely divided form; upon subsequent washing with alcohol, the mercuric iodide is removed, leaving the insoluble mercurous salt intimately

mixed with finely divided mercury, and of a green color. Similar results are apt to occur if mercurous iodide be precipitated from a strong neutral solution of mercurous nitrate by means of potassium iodide, hence the Pharmacopœia directs a dilute acid solution.

Mercurous iodide has been associated with syrup of ferrous iodide in prescriptions, but such mixtures are incompatible, metallic mercury being deposited, a reaction similar to that explained above taking place, and mercuric iodide held in solution by the ferrous iodide.

Corrosive Mercuric Chloride. $HgCl_2$. This compound, more familiarly known as corrosive sublimate, is obtained by sublimation of an intimate mixture of mercuric sulphate and sodium chloride, both in the form of powder. Mercuric chloride is formed as the result of mutual decomposition; thus, $HgSO_4 + 2NaCl = HgCl_2 + Na_2SO_4$. The heat necessary for the process is apt to decompose some of the mercuric sulphate with the formation of mercurous chloride, which is volatilized and sublimed along with the mercuric salt. The British Pharmacopœia directs the addition of a small portion of manganese dioxide to the mixture before subliming it, for the purpose of preventing the formation of mercurous salt.

Commercial mercuric chloride occurs in heavy crystalline masses and is usually contaminated somewhat with calomel, hence perfectly clear solutions can rarely be obtained, even with distilled water. For dispensing purposes, only the chemically pure article, obtained by recrystallization should be used.

Aqueous solutions of mercuric chloride, if exposed to light, gradually undergo decomposition, liberating hydrochloric acid and depositing calomel. The presence of ammonium chloride, however, prevents the change.

The pharmacopœial test for the presence of arsenic in mercuric chloride, depends upon the solubility of arsenic sulphide in ammonia water and its subsequent precipitation by hydrochloric acid, mercuric sulphide being insoluble in ammonia water.

Mercuric Cyanide. $HgCN_2$. This salt may be prepared pure by dissolving mercuric oxide (preferably the yellow) in hydrocyanic acid, avoiding an excess of the oxide, which would form a basic compound; a slight excess of the acid is not objectionable, as it will be dissipated on evaporation of the solution. Simple agitation suffices to effect solution, the liquid being then concentrated and set aside, in a dark, cool place, to crystallize. The resulting crystals must be both dried and preserved with exclusion of light, as the salt will otherwise darken rapidly.

Mercuric cyanide is the only cyanide of the heavy metals completely soluble in water; its solution is colorless, without odor, and differs from a solution of mercuric chloride in not being precipitated by alkali hydroxides or carbonates, silver nitrate, and potassium iodide. It is a very poisonous compound, rarely used in medicine.

RED MERCURIC IODIDE. HgI_2. This salt is prepared by mutual decomposition between mercuric chloride and potassium iodide, the official directions being to pour a solution of 40 Gm. of the former salt and a solution of 50 Gm. of the latter, simultaneously, into a large volume of water, with active stirring, when the following reaction occurs: $HgCl_2 + 2KI = HgI_2 + 2KCl$. The official formula employs the two salts very nearly in the proportions indicated in the foregoing equation, which are 4 and 4.898 respectively; an excess of either salt must be avoided, since loss by formation of a soluble compound would result, an excess of potassium iodide producing potassium mercuric iodide ($HgI_2 + 2KI$) and an excess of mercuric chloride causing the formation of mercuric iodochloride ($HgI_2 + 2HgCl_2$ or $Hg_3I_2Cl_4$).

Mercuric iodide is dimorphous, occurring crystallized both in the form of scarlet-red quadratic octahedra and yellow rhombic prisms, but the Pharmacopœia recognizes the salt only in the form of an amorphous scarlet-red powder, which is obtained by the official method of preparation. When exposed to light, mercuric iodide gradually becomes paler in color, and should therefore be preserved in dark bottles. It is soluble in solutions of metallic iodides and sodium thiosulphate, as well as alcohol, olive oil, castor oil, chloroform, glycerin, and glacial acetic acid, forming colorless solutions in each case.

YELLOW MERCURIC OXIDE. HgO. The official formula for the preparation of this compound directs that a strong solution of 100 Gm. of mercuric chloride be poured slowly, with constant stirring, into a dilute solution of 40 Gm. of 90 per cent. sodium hydroxide; amorphous mercuric oxide is precipitated while sodium chloride enters into solution. The mixture is allowed to stand, at a moderate temperature, for an hour, to facilitate complete decomposition, after which the liquid is decanted and the precipitate repeatedly washed until free from alkali, drained and dried on paper, in a dark place, at a temperature of 30° C. (86° F.).

Mercuric salts do not form hydroxides when added to alkali hydroxides, but mercuric oxide is precipitated instead, as shown by the equation, $HgCl_2 + 2NaOH = HgO + 2NaCl + H_2O$. It is important that the alkali be used in excess, otherwise a dark-colored oxychloride will be formed, hence the mercuric chloride solution is poured into the soda solution in the official process. From the above equation, it will be seen that 1 molecule (or 270.54 parts) of mercuric chloride requires 2 molecules (or 79.92 parts) of sodium hydroxide for complete precipitation; hence 100 Gm. $HgCl_2$ will require 29.5 Gm. NaOH; official soda containing 90 per cent. of NaOH, the necessary excess of alkali is assured in the formula of the Pharmacopœia, as 90 per cent. of 40 Gm. is 36 Gm. It is essential that the soda used be free from carbonate, otherwise mercuric carbonate will be formed. Potassa may be used in place of soda, but ammonia is

inadmissible, owing to the formation of ammoniated mercury. In order to insure a bright orange-yellow product, heat and light must be excluded during precipitation and drying; unless protected from light the color of the oxide gradually darkens on keeping, and, if exposed to direct sunlight, decomposition rapidly occurs.

Yellow mercuric oxide, being in a very fine state of division, is more active and more sensitive than the red oxide; it is chemically identical with the latter, but differs from it in the molecular arrangement of its particles, being devoid of all crystalline structure. When digested with a solution of oxalic acid, yellow mercuric oxide forms white mercuric oxalate, while the red oxide remains unaffected.

Red Mercuric Oxide. HgO. Although the name "red precipitate" is commonly applied to this compound, it is never obtained by precipitation but always by calcination. As a rule, mercuric nitrate is triturated with metallic mercury until the latter is extinguished; the mixture is then heated, in a porcelain dish, until yellowish or reddish vapors cease to be evolved and mercuric oxide remains. The metallic mercury is oxidized at the expense of the nitric acid expelled from the mercuric nitrate, and the process may be illustrated by the following equation: $2Hg(NO_3)_2+Hg_2=4HgO+4NO_2$.

Red mercuric oxide occurs as a crystalline powder or in crystalline scales of an orange-red color, and by trituration with alcohol is gradually converted into a yellowish-red powder. When exposed to light it darkens in color, but more slowly than the yellow oxide, and, unlike the latter, it is not affected by hot solution of oxalic acid.

Yellow Mercuric Subsulphate. $Hg(HgO)_2SO_4$. A basic mercuric sulphate, prepared by pouring normal mercuric sulphate into boiling water, whereby the latter salt suffers decomposition. The official directions are to prepare normal mercuric sulphate by gently heating a mixture of mercury 100 Gm., sulphuric acid 30 Cc., nitric acid 25 Cc., and water 40 Cc., until reddish fumes are no longer evolved, during which operation the following reaction occurs: $Hg_3+3H_2SO_4+2HNO_3=3HgSO_4+4H_2O+2NO$. The resulting mixture is heated in a porcelain dish, on a sand-bath, until a dry white mass remains, which is powdered and added, in small quantities at a time, to 2000 Cc. of boiling water, after which the mixture is kept boiling for ten minutes. The liquid is decanted, the precipitate washed with warm water, until free from acid, and then dried with a moderate heat.

The addition of nitric acid is not essential, but facilitates the formation of mercuric sulphate at a lower temperature, cold and even moderately warm sulphuric acid having no effect on mercury, especially in the presence of water. When normal mercuric sulphate is added to boiling water decomposition results, basic sulphate being precipitated, while acid sulphate remains in solution; thus, $5HgSO_4+2H_2O=Hg(HgO)_2SO_4+2HgH_2(SO_4)_2$; the yield depends upon the temperature and the volume of water used.

Yellow mercuric subsulphate is commercially better known by the name "turpeth mineral." It should be completely soluble in 10 parts of hydrochloric acid, showing the absence of mercurous and lead salts.

SOLUTION OF MERCURIC NITRATE. An acid liquid containing about 60 per cent. of mercuric nitrate and about 11 per cent. of free nitric acid. This, the only fluid preparation of mercury officially recognized, is made by solution of 40 Gm. of mercuric oxide in a mixture of 45 Gm. of nitric acid and 15 Gm. of water. According to the equation, $3HgO+8HNO_3=3Hg(NO_3)_2+2NO+4H_2O$, 647.24 parts of mercuric oxide require 503.12 parts of absolute nitric acid to form 970.74 parts of mercuric nitrate; hence 40 Gm. will require 23.32 Gm. of absolute, or 34.3 Gm. of official, nitric acid and will yield 59.99 Gm. of the salt. Moderate dilution of the acid with water is advantageous, facilitating the solution of the newly formed salt.

This very corrosive preparation, rarely used and then only for external application, requires great care in handling. It is also known by the name acid nitrate of mercury and is the densest solution of the Pharmacopœia, having a specific gravity of 2.100, at 15° C. (59° F.).

Among the non-official compounds of mercury of interest to the pharmacist, the following may be mentioned:

MERCURIC SULPHATE. $HgSO_4$. This salt, which has already been mentioned in connection with mercurous and mercuric chloride and mercuric subsulphate, may be prepared either by the process mentioned under the latter salt or by heating mercury with sulphuric acid and evaporating the mixture to dryness, when a crystalline product will be obtained; water and sulphur dioxide are eliminated during the operation.

MERCUROUS TANNATE. This compound is prepared by triturating freshly prepared and finely powdered mercurous nitrate with a mixture of tannin and water until a homogeneous smooth mass is obtained. The mass is mixed with a large volume of water, and the green precipitate is washed with water until no trace of nitric acid remains, after which it is dried on porous tiles, at a temperature not exceeding 40° C. (104° F.).

MERCURIC CARBOLATE OR PHENATE. Of the two preparations occurring under this name, the so-called normal mercuric phenate, or mercuric diphenate, $Hg(C_6H_5O)_2$, should be dispensed, being a stable preparation. It is obtained by mixing, with constant stirring, an alcoholic solution of mercuric chloride with an alcoholic solution of carbolic acid and potassium hydroxide, draining the yellowish-colored

precipitate, washing it with hot water acidulated with acetic acid and recrystallizing from hot alcohol.

MERCURIC SALICYLATE. $HgOC_7H_4O_2$. This salt may be prepared by adding salicylic acid to freshly precipitated mercuric oxide rubbed into a smooth paste with water and heating the mixture on a water-bath until a snow-white mass remains, free from a yellow tint, which is then washed with warm water to remove excess of acid, drained and dried. The resulting amorphous product constitutes secondary or basic mercuric salicylate, which is the salt generally employed. Normal mercuric salicylate, $Hg(C_7H_5O_3)_2$, can be obtained by precipitating a solution of mercuric chloride with sodium salicylate in the cold; the resulting product is readily decomposed by heat.

CHAPTER L.

THE COMPOUNDS OF ANTIMONY, ARSENIC AND BISMUTH.

While at one time the preparations of antimony formed an important part of the physician's armamentarium, they are but rarely prescribed at the present time; those of arsenic and bismuth, however, are still looked upon as valuable remedial agents. The Pharmacopœia recognizes five chemical compounds and three pharmaceutical preparations of antimony, two compounds of arsenic, besides four arsenical solutions and four compounds of bismuth, as shown by the following list:

Official English Name.	Official Latin Name.
Antimony and Potassium Tartrate.	Antimonii et Potassii Tartras.
Antimony Oxide.	Antimonii Oxidum.
Antimony Sulphide.	Antimonii Sulphidum.
Purified Antimony Sulphide.	Antimonii Sulphidum Purificatum.
Sulphurated Antimony.	Antimonium Sulphuratum.
Compound Pills of Antimony.	Pilulæ Antimonii Compositæ.
Antimonial Powder.	Pulvis Antimonialis.
Wine of Antimony.	Vinum Antimonii.
Arsenic Iodide.	Arsenii Iodidum.
Arsenous Acid.	Acidum Arsenosum.
Solution of Arsenous Acid.	Liquor Acidi Arsenosi.
Solution of Arsenic and Mercuric Iodide.	Liquor Arsenii et Hydrargyri Iodidi.
Solution of Potassium Arsenite.	Liquor Potassii Arsenitis.
Solution of Sodium Arsenate.	Liquor Sodii Arsenatis.
Bismuth Citrate.	Bismuthi Citras.
Bismuth and Ammonium Citrate.	Bismuthi et Ammonii Citras.
Bismuth Subcarbonate.	Bismuthi Subcarbonas.
Bismuth Subnitrate.	Bismuthi Subnitras.

The Compounds of Antimony.

Antimony and Potassium Tartrate. $2K\,SbO)C_4H_4O_6 - H_2O$. This salt, which has been known for over 250 years, is prepared by boiling a mixture of acid potassium tartrate and antimonous oxide with water for some time, filtering the liquid, concentrating by evaporation and crystallizing. The British Pharmacopœia directs that a paste be made of the antimonous oxide, cream of tartar, and a small quantity of water, which is set aside for twenty-four hours to allow combination to take place, after which more water is added and the mixture boiled for fifteen minutes to bring all the newly formed double tartrate into solution.

If pure materials be used, the full theoretical yield is generally obtained, but, if the antimonous oxide be contaminated with oxychloride, some of the salt will be lost by refusing to crystallize in

the acid liquid. The following equation, $Sb_2O_3 + 2KHC_4H_4O_6 = 2K(SbO)C_4H_4O_6 + H_2O$, explains the formation of antimony and potassium tartrate, the univalent group SbO replacing the hydrogen in the acid potassium tartrate, water being formed at the same time.

The synonyms, tartar emetic and tartrated antimony, are given in the Pharmacopœia for this compound, the former being the name generally employed in commerce. The salt is recognized in the British Pharmacopœia as *antimonium tartaratum* and in the German Pharmacopœia as *tartarus stibiatus*. It is generally sold in powder form, obtained by trituration of the crystals. Aqueous solutions of tartar emetic gradually develop fungi, and, on that account, cannot be kept on hand for any length of time, nor can they be mixed with strongly alcoholic liquids without precipitation, as the salt is totally insoluble in alcohol.

The Pharmacopœia requires absolute purity for tartar emetic, the valuation being made with decinormal iodine solution in the presence of sodium bicarbonate and starch solution. The iodine, acting as an oxidizing agent, converts the antimonyl into meta-antimonic acid, hydriodic acid and sodio-potassium tartrate being also formed; the object of adding sodium bicarbonate is to neutralize the two newly formed acids, thereby preventing decomposition of the hydriodic acid by the meta-antimonic acid, which would liberate iodine and thus vitiate the end-reaction. The equation, $(2K(SbO)C_4H_4O_6 + H_2O) + I_4 + 8NaHCO_3 = 2NaSbO_3 + 4NaI + 2KNaC_4H_4O_6 + 8CO_2 + 6H_2O$, shows that each molecule (or 662.42 parts) of crystallized tartar emetic requires 4 atoms (or 506.12 parts) of iodine for complete oxidation of the antimony present, hence 0.331 Gm. will require 0.25306 Gm. of iodine or 20 Cc. of its decinormal solution, for $662.42 : 506.12 :: 0.331 : 0.25306$ and $0.25306 \div 0.012653 = 20$.

In the official test for the presence of arsenic the addition of tinfoil should be omitted, as otherwise metallic antimony will be precipitated in a finely divided form, thus vitiating the reliability of the test, which depends upon the separation of metallic arsenic by the stannous chloride.

ANTIMONY OXIDE. Antimonous Oxide. Antimony Trioxide. Sb_2O_3. This compound is obtained by first preparing a solution of antimony trichloride, $SbCl_3$, from antimonous sulphide and hydrochloric acid, pouring this into water, whereby antimony oxychloride, $2SbCl_3 + 5Sb_2O_3$ (known as powder of Algaroth), is precipitated, which is then repeatedly washed with water and mixed with a solution of sodium carbonate, converting the oxychloride into pure oxide, with elimination of carbon dioxide and formation of sodium chloride, thus, $(2SbCl_3 + 5Sb_2O_3) + 3Na_2CO_3 = 6Sb_2O_3 + 6NaCl + 3CO_2$. In place of sodium carbonate, ammonia water is frequently employed. After proper washing of the oxide, it is dried at a temperature not exceeding 100° C. (212° F.), so as to avoid the formation of higher oxides.

Antimony oxide is used in the manufacture of tartar emetic and antimonial powder.

ANTIMONY SULPHIDE. Sb_2S_3. Under this name the Pharmacopœia recognizes native antimony sulphide, obtained from the ore stibnite, by fusion, whereby it is freed from accompanying infusible sulphides, siliceous matter, etc. It is the source of the other antimony compounds, and is known in commerce as black or crude antimony, occurring both in cone-shaped masses and powder-form of a steel-gray color, and having a metallic lustre. It is contaminated with variable proportions of arsenic trisulphide.

PURIFIED ANTIMONY SULPHIDE. Sb_2S_3. In the official process for the purification of antimony sulphide, only the finely divided article, obtained by elutriation, is used, which is macerated for five days, in a closed vessel, with diluted ammonia water, with frequent agitation; the liquid is then decanted and the residue repeatedly washed with water and dried at a gentle heat. Antimonous sulphide is always associated with arsenous sulphide, which it is intended to remove by the treatment with ammonia water, wherein it is soluble. Hager and others suggest that ammonium carbonate be added to the mixture, after two or three days' maceration, with a view of dissolving less of the antimonous sulphide, which, although soluble to some extent in the ammonia water, is totally insoluble in solution of ammonium carbonate.

Purified antimony sulphide differs in appearance from the crude sulphide, being a lustreless powder of dark-gray or grayish-black color.

In the official test for the absence of more than $\frac{1}{10}$ per cent. of arsenic, all antimonous and arsenous sulphide present in the sample is oxidized by cautious ignition with sodium nitrate, sodium meta-antimonate, $NaSbO_3$, and sodium pyro-arsenate, $Na_4As_2O_7$ being formed. Upon addition of water, the latter salt is changed into sodium ortho-arsenate, Na_2HAsO_4, and readily dissolves; the former salt is insoluble in cold and only slowly soluble in boiling water. The filtrate, containing all sodium arsenate, is boiled with nitric acid to convert the sodium nitrite (due to reduction of the sodium nitrate in the previous operation) into sodium nitrate, after which silver nitrate is added, whereby silver arsenate, Ag_3AsO_4, is formed by double decomposition. Upon carefully pouring a little ammonia water on top of the solution, so as to form a neutral liquid at the line of contact, a white cloud will be observed if only a very minute quantity of arsenic was present in the sample of antimony sulphide, but, if more than $\frac{1}{10}$ per cent. was present, the silver arsenate will separate as a flesh-colored or reddish-brown precipitate. Silver arsenate is soluble both in nitric acid and ammonia water, but is insoluble in neutral liquids, hence the separation will appear only at the line of contact.

SULPHURATED ANTIMONY. This preparation consists chiefly of precipitated antimonous sulphide mixed with small and variable quantities of antimonous oxide. The Pharmacopœia directs that purified native antimony sulphide be boiled with about twelve times its weight of a 5 per cent. solution of sodium hydroxide, for two hours, the liquid to be immediately strained, after which diluted sulphuric acid is added, drop by drop, as long as it causes precipitation. The precipitate is washed with hot water to remove all sulphates, and then dried at a temperature not exceeding 25° C. (77° F.).

Crystalline antimony sulphide is not affected by cold alkaline liquids, but, upon boiling such a mixture, a solution is formed of alkali meta-antimonite and sulpho-antimonite, as shown by the following equation: $Sb_2S_3 + 4NaOH = NaSbO_2 + Na_3SbS_3 + 2H_2O$. This solution, which is colorless, is separated by straining, and, upon the addition of sulphuric acid, is decomposed, amorphous antimonous sulphide being precipitated, thus: $NaSbO_2 + Na_3SbS_3 + 2H_2SO_4 = Sb_2S_3 + 2Na_2SO_4 + 2H_2O$. Small quantities of antimonous oxide are also formed and remain mixed with the sulphide. While the precipitated antimonous sulphide occurs as a reddish-brown amorphous powder, it does not differ in its chemical composition from the black native sulphide, which is crystalline.

The name Kermes Mineral is also officially applied to this preparation, which is not identical with the commercial Golden Sulphur of Antimony, recognized, in the British Pharmacopœia, under the title of *sulphurated antimony*. To the latter preparation the German Pharmacopœia applies the name *stibium sulphuratum aurantiacum;* it consists chiefly of antimony pentasulphide, Sb_2S_5, with possible admixtures of antimony trisulphide and oxide. Golden sulphur of antimony is of an orange-red color and is prepared in a similar manner to Kermes Mineral, except that sulphur is added to the mixture of black antimony sulphide and solution of soda. Upon boiling this mixture, sodium sulphide, Na_2S, is formed, which, reacting with sulphur and antimonous sulphide, yields sodium sulpho-antimonate, a compound known as Schlippe's salt, thus: $Sb_2S_3 + 3Na_2S + S_2 = 2Na_3SbS_4$; this is decomposed by the addition of diluted sulphuric acid to its solution, when antimony pentasulphide is precipitated, hydrogen sulphide escaping and sodium sulphate remaining in solution, thus: $2Na_3SbS_4 + 3H_2SO_4 = Sb_2S_5 + 3H_2S + 3Na_2SO_4$. Any admixture of antimony trisulphide is due to the possible formation of sodium sulpho-antimonite, Na_3SbS_3, during the boiling of the alkaline liquid, and its subsequent decomposition by the acid.

The Compounds of Arsenic.

ARSENIC IODIDE. AsI_3. Arsenic is capable of forming several compounds with iodine, of which, the one indicated by the above formula and more particularly known as arsenic triiodide, is alone recognized in the Pharmacopœia. It may be obtained by fusing, in

a loosely stoppered test-tube or bottle, a mixture of 4 Gm. of metallic arsenic and 20 Gm. of iodine and pouring the melted mass on a porcelain slab to cool. Some manufacturers prefer to make it by adding finely powdered metallic arsenic to a solution of iodine in carbon disulphide, until all color of iodine has disappeared, then concentrating and crystallizing the solution.

Arsenic iodide must be carefully protected from air and light, otherwise it undergoes decomposition, losing iodine and becoming insoluble in water. Its aqueous solution gradually changes, arsenous and hydriodic acids being formed. The chief use made of the compound is in the preparation of Donovan's Solution.

ARSENOUS ACID. As_2O_3. This compound has been known for centuries, and, although it is still designated as an acid by the Pharmacopœia, the names, arsenic trioxide, arsenous oxide, or arsenous anhydride, seem more in conformity with its true character, since the dry substance evinces no acid properties whatever, and, even dissolved in water, shows only a very feeble acid reaction. It is obtained chiefly as a by-product in the roasting of tin, cobalt, and nickel ores, and is subsequently purified by sublimation.

Arsenic trioxide occurs in two distinct varieties, an amorphous, vitreous (glass-like) form and a crystalline, opaque, porcelain-like variety, the former being gradually converted into the latter upon exposure to moist air. The solubility of the two varieties in water differs materially, the vitreous being nearly three times as soluble as the porcelain-like variety, but the solubility of both is increased by the presence of hydrochloric acid or alkali hydroxides and carbonates, alkali arsenites being formed in the last two cases. When arsenic trioxide is dissolved in water, arsenous acid is formed, thus: $As_2O_3 + 3H_2O = 2H_3AsO_3$, which, however, cannot be isolated, as upon evaporation of the solution arsenic trioxide is again obtained. While alcohol exerts but a slight solvent effect on either variety, glycerin will dissolve about one-fifth of its weight of both, again depositing a portion however upon dilution with water, and oil of turpentine dissolves the vitreous, but not the opaque variety.

Although the synonym, *white arsenic*, is officially recognized, it should be borne in mind that the commercial product in powder form, known as white arsenic, is usually impure and unfit for pharmaceutical purposes. Arsenic trioxide should never be purchased in powder form, except in bottles bearing on the label the name of some reputable manufacturer or dealer.

The quality of arsenic trioxide can be readily ascertained by titration with decinormal iodine solution, which converts arsenous into arsenic acid. The Pharmacopœia requires that official arsenous acid shall contain not less than 98.8 per cent. of As_2O_3; 0.1 Gm. dissolved in 20 Cc. of water together with 1.0 Gm. of sodium bicarbonate should decolorize at least 20 Cc. $\frac{N}{10}$ I solution, the following

reaction taking place: $As_2O_3+8NaHCO_3+I_4+2H_2O=2Na_2HAsO_4+4NaI+8CO_2+5H_2O$. Since one molecule (or 197.68 parts) of arsenic trioxide requires 4 atoms (or 506.12 parts) of iodine for complete oxidation, each Cc. of $\frac{N}{10}$ I solution must correspond to 0.004942 Gm. As_2O_3 and 20 Cc. equal 0.098848 Gm., which is 98.8 per cent. of 0.1 Gm. The addition of sodium bicarbonate is made for the purpose of neutralizing the acids formed, thus preventing the constant liberation of iodine through decomposition of the hydriodic acid by the arsenic acid.

Solution of Arsenous Acid. This is simply a solution of arsenous acid in water, containing also 5 per cent. of official diluted hydrochloric acid, which latter is added solely to facilitate solution of the arsenous oxide, no chemical action taking place. Formerly this preparation was called solution of chloride of arsenic, under a false impression; arsenous chloride, As_2Cl_6, can be obtained by treating arsenic trioxide with strong hydrochloric acid or by distilling arsenous and hydrochloric acids together; but, upon being dissolved in water, it is again split up into the compounds from which it was made.

The Pharmacopœia requires that the solution shall contain, in every Cc., 0.010 Gm. of official arsenous acid (corresponding to about 4.86 grains in every fluidounce), which is determined by titration with decinormal iodine solution, as in the case of the valuation of arsenic trioxide. 24.7 Cc. of the official solution, containing 0.244 Gm. of absolute As_2O_3 (1 Gm. of 98.8 per cent. arsenic trioxide in 100 Cc.) will require not less than 49.5 Cc. $\frac{N}{10}$ I solution, each Cc. of which corresponds to 0.004942 Gm. As_2O_3, for complete oxidization. The reaction has been fully explained in the preceding article.

Solution of Arsenic and Mercuric Iodide. Red mercuric iodide, which alone is almost insoluble in water, becomes soluble in the presence of arsenic iodide, and, in preparing the above solution, the two iodides are triturated together and then mixed with water, when solution readily takes place. It is important that the arsenic iodide be of good quality, otherwise an insoluble residue will remain. The solution contains, in every Cc., 0.010 Gm. each of arsenic and mercuric iodide (corresponding to about 4.86 grains of each in every fluidounce), and should be preserved in small, well-stoppered vials, in a dark place, as it is prone to decomposition. When freshly made it is of a pale-straw color, and, if this changes to reddish or red, iodine has been liberated, and the solution should not be dispensed.

This preparation is better known as Donovan's Solution, and was at one time considered a very valuable remedial agent, but is little used at present. On account of the powerful action of arsenic and

mercuric iodides this solution was formerly called by some physicians *The Three Samsons of Medicine.*

SOLUTION OF POTASSIUM ARSENITE. This preparation, popularly known as Fowler's Solution, is probably the most extensively employed of all arsenical compounds. It is made by heating arsenic trioxide and potassium bicarbonate with a small quantity of water until perfect solution has been effected, which when cold is diluted with water, and compound tincture of lavender added. The use of a small quantity of water is favorable to chemical union between the alkali and feeble acid; the nature of the compound depends upon the proportions used; thus, in the formula of the United States Pharmacopœia, one part of arsenic trioxide and two parts of potassium bicarbonate will produce the following reaction: $4KHCO_3 + As_2O_3 + 3H_2O = 2K_2HAsO_3 + 4H_2O + 4CO_2$, monobasic potassium ortho-arsenite being formed, while the preparations of the British and German Pharmacopœias, made with equal weights of arsenic trioxide and potassium carbonate, contain potassium meta-arsenite, as shown by the equation, $As_2O_3 + K_2CO_3 = 2KAsO_2 + CO_2$.

The solution is most conveniently prepared in a test-tube of sufficient capacity or a small long-neck flask, whereby the evaporation of water is materially reduced; the dilution should not be made until the liquid is cold. Solution of potassium arsenite is apt to develop fungi in the course of time, and if an excess of alkali be present, as in the British and German preparations, the arsenous acid is gradually converted into arsenic acid; it is, therefore, better not to keep the solution on hand in large quantities. While the preparations of the United States and British Pharmacopœias are colored reddish by the compound tincture of lavender added, those of the German and French Pharmacopœias are colorless. The term *liquor arsenicalis* is officially used in Great Britain to designate this solution.

Owing to its very poisonous nature, Fowler's Solution should never be dispensed without a physician's prescription, and, although sometimes called for by the public, pharmacists should refuse to sell it, for their own protection as well as that of others.

The official solution of potassium arsenite must contain 1 Gm. of official arsenous acid in every 100 Cc. of solution, corresponding to 4.86 grains in each fluidounce, which is determined with iodine, exactly as in the case of solution of arsenous acid.

SOLUTION OF SODIUM ARSENATE. An aqueous solution of sodium arsenate, containing 0.010 Gm. of anhydrous salt in each Cc. The object of using anhydrous sodium arsenate is to insure uniformity of strength in the finished product, as the commercial salt contains variable proportions of water of crystallization (see page 443); the temperature used for desiccation should not be carried beyond 149° C. (300° F.), in order to avoid changing the sodium ortho-arsenate into pyro-arsenate.

This preparation is not identical with Pearson's Arsenical Solution, recognized in the French Pharmacopœia, and prepared by dissolving 1 part of crystallized sodium arsenate in 600 parts of water. As Pearson's Solution is sometimes prescribed in this country, it should be borne in mind that the solution of sodium arsenate of the United States Pharmacopœia is about ten times as strong as the French preparation bearing Dr. Pearson's name.

The Compounds of Bismuth.

BISMUTH CITRATE. $BiC_6H_5O_7$. This salt is prepared by boiling a mixture of 100 Gm. of bismuth subnitrate and 70 Gm. of citric acid, with 400 Cc. of water, until a drop of the mixture forms a clear solution with ammonia water, after which it is diluted with a large volume of water, allowed to subside, and repeatedly washed with water by decantation, until free from nitric acid, and dried with the aid of a gentle heat.

The use of a small quantity of water is advantageous for the complete conversion of the bismuth subnitrate into citrate; the reaction taking place may be illustrated by the following equation: $(BiONO_3 + H_2O) + (H_3C_6H_5O_7 + H_2O) = BiC_6H_5O_7 + HNO_3 + 3H_2O$, which shows that 100 Gm. of bismuth subnitrate require 68.75 Gm. of crystallized citric acid (for 304.71 : 209.5 :: 100 : 68.75), which leaves a very slight excess of citric acid in the official formula. The composition of bismuth subnitrate may differ, however, from the formula assigned to it in this reaction (see Bismuth Subnitrate).

The only use made of the normal bismuth citrate in pharmacy is in the manufacture of the soluble compound next mentioned.

BISMUTH AND AMMONIUM CITRATE. The official formula for this preparation directs that ammonia water shall be gradually added to a smooth paste made of normal bismuth citrate and twice its weight of water, until a perfect solution has been effected, which is strained, concentrated on a water-bath to a syrupy consistency, and spread upon plates of glass to dry. A slight excess of ammonia water will be advantageous, in order to maintain a neutral or faintly alkaline reaction during evaporation of the solution, as some ammonia will be lost and an acid condition would cause precipitation.

The exact composition of this compound cannot be definitely stated. By some, the view is held that, by the action of ammonia, bismuthous hydroxide is formed, which is held in solution by the ammonium citrate simultaneously produced, giving the salt the composition indicated by the formula, $Bi(OH)_3 + (NH_4)_3C_6H_5O_7 + Aq.$; others have suggested that the composition may be expresed thus: $BiC_6H_5O_7 + NH_4OH + H_2O$.

The scaled salt obtained by the official process slowly loses ammonia, unless preserved in tightly stoppered bottles, thereby becom-

[illegible] When such a solution, the minute addition of a few drops of ammonia water or [illegible] usually effects a perfect solution, as in similar cases of the [illegible].

The British Pharmacopœia requires a solution of bismuth and ammonium citrate, which is prepared by dissolving 4 grains of bismuth citrate in 100 fluidounces of water by means of ammonia. It is prepared as described above, and is known in England as [illegible].

BISMUTH SUBCARBONATE. The first step necessary in the manufacture of this compound is the preparation of a solution of pure bismuth nitrate, which is then decomposed by means of a hot solution of sodium carbonate. When metallic bismuth is treated with a hot and concentrated solution of nitric acid, $Bi(NO_3)_3$ is formed, and the arsenic, which is almost invariably present in bismuth, is converted into arsenic acid, and combining with bismuth forms bismuth arsenate, $BiAsO_4$. In order to rid the solution of the latter salt it is diluted with water to incipient turbidity and set aside for 24 or 36 hours, when nearly all the bismuth arsenate will have been deposited, being less soluble than the nitrate; by adding an excess of ammonia water to the clear solution all bismuth will be precipitated as bismuthous hydroxide, ammonium nitrate and arsenate remaining in solution. After washing the precipitate until the washings are tasteless, it is redissolved in nitric acid, and this solution of purified bismuth trinitrate slowly added, with constant stirring, to a solution of sodium carbonate, when the following reaction occurs: $2Bi(NO_3)_3 + 3Na_2CO_3 + H_2O = BiO.CO_3 + H_2O + 6NaNO_3 + 2CO_2$. The final precipitate, consisting of basic bismuth carbonate, is thoroughly washed with water and dried with moderate heat.

The exact composition of bismuth subcarbonate depends upon the degree of dilution of the sodium carbonate solution and the temperature at which the bismuth nitrate is added and the final precipitate dried. The Pharmacopœia demands that bismuth subcarbonate, upon being heated to redness, shall leave a yellow residue of bismuth oxide, Bi_2O_3, weighing from 87 to 91 per cent. of the original weight of the sample used; a salt of the above composition will yield 88.27 per cent. of oxide, and probably represents the average commercial salt of good quality. In England the salt is known as bismuth carbonate, the British Pharmacopœia directing the use of ammonium carbonate in place of sodium carbonate, and assigning the formula $2Bi_2O_3CO_3 + H_2O$ to the finished product.

BISMUTH SUBNITRATE. A part of the process of manufacture of this salt has already been detailed in the preceding article. When a solution of purified bismuth trinitrate is poured into water, precipitation of a basic salt at once takes place, the nitric acid liberated, however, retaining some of the normal nitrate in solution. As in

the case of the subcarbonate, the composition of the precipitate will vary with the volume and temperature of the water used, and also the temperature at which the salt is dried. If precipitated with cold water, bismuth subnitrate is supposed to have the composition $BiO(NO_3) + H_2O$; but if washed with water for some time, a more basic salt results, probably of the composition $BiO(NO_3) + H_2O + Bi(OH)_3$.

The Pharmacopœia requires that official bismuth subnitrate shall yield, when heated to redness, from 79 to 82 per cent. of its weight of bismuth oxide; such a salt is represented by the formula of the more basic salt given above, yielding the maximum amount of oxide.

Although a basic salt, bismuth subnitrate, mixed with water, shows an acid reaction, and should not be dispensed in mixtures containing alkali carbonates or bicarbonates as decomposition (often with explosive violence) will result (see also page 298).

In continental Europe the salt is frequently prescribed under the name *magisterium bismuthi.*

Among the non-official compounds of bismuth the following are of interest:

Bismuth Oxide. Bi_2O_3. This compound may be conveniently prepared by boiling bismuth subnitrate with solution of potassa or soda, washing the resulting precipitate well with water, and finally drying it on a boiling water-bath. It is officially recognized in the British Pharmacopœia. Bismuth oxide is of yellowish-white color, and is used in the preparation of bismuth oleate.

Bismuth Salicylate. $Bi(C_7H_5O_3)_3 + Bi_2O_3$. This salt, which, as shown by the formula, is a basic compound, is best prepared by digesting freshly precipitated bismuth hydroxide with salicylic acid at ordinary room temperature for 48 hours, then washing with small quantities of cold water until all free acid has been removed, and finally drying in a dark place at a low temperature. It occurs as a cream-colored odorless, tasteless, amorphous powder, which must be protected from light.

Bismuth Subgallate. This compound, which is also known as Dermatol, is prepared by dissolving crystallized normal bismuth nitrate in glacial acetic acid, diluting the solution with water, and adding, with constant stirring, a warm solution of gallic acid. The resulting precipitate is washed with water until free from nitric acid, and dried at 100° C. (212° F.). It is an impalpable saffron-yellow, odorless powder, permanent in the air, and insoluble in all ordinary solvents.

CHAPTER LI.

THE COMPOUNDS OF COPPER, LEAD, ZINC, GOLD, AND SILVER.

WHILE copper and gold each furnish but one compound recognized in the Pharmacopœia, the official salts of lead, silver, and zinc are more numerous and of greater importance, as may be seen by the following list:

Official English Name.	Official Latin Name.
Copper Sulphate,	Cupri Sulphas.
Lead Acetate,	Plumbi Acetas.
Lead Carbonate,	Plumbi Carbonas.
Lead Iodide,	Plumbi Iodidum.
Lead Nitrate,	Plumbi Nitras.
Lead Oxide,	Plumbi Oxidum.
Lead Plaster,	Emplastrum Plumbi.
Cerate of Lead Subacetate,	Ceratum Plumbi Subacetatis.
Solution of Lead Subacetate,	Liquor Plumbi Subacetatis.
Ointment of Lead Carbonate,	Unguentum Plumbi Carbonatis.
Ointment of Lead Iodide,	Unguentum Plumbi Iodidi.
Zinc Acetate,	Zinci Acetas.
Zinc Bromide,	Zinci Bromidum.
Precipitated Zinc Carbonate,	Zinci Carbonas Præcipitatus.
Zinc Chloride,	Zinci Chloridum.
Zinc Iodide,	Zinci Iodidum.
Zinc Oleate,	Zinci Oleatum.
Zinc Oxide,	Zinci Oxidum.
Zinc Phosphide,	Zinci Phosphidum.
Zinc Sulphate,	Zinci Sulphas.
Zinc Valerianate,	Zinci Valerianas.
Solution of Zinc Chloride,	Liquor Zinci Chloridi.
Ointment of Zinc Oxide,	Unguentum Zinci Oxidi.
Gold and Sodium Chloride,	Auri et Sodii Chloridum.
Silver Cyanide,	Argenti Cyanidum.
Silver Iodide,	Argenti Iodidum.
Silver Nitrate,	Argenti Nitras.
Diluted Silver Nitrate,	Argenti Nitras Dilutus.
Moulded Silver Nitrate,	Argenti Nitras Fusus.
Silver Oxide,	Argenti Oxidum.

The Compounds of Copper.

COPPER SULPHATE. $CuSO_4+5H_2O$. The crude salt, known in commerce as blue vitriol, is not suited for pharmaceutical purposes, on account of the impurities (iron and other metals) present; and, as these cannot be removed by simple recrystallization, a better article may be obtained by direct solution of metallic copper in diluted sul-

phuric acid aided by a little nitric acid, the following reaction taking place: $Cu_3 - 3H_2SO_4 - 2HNO_3 = 3CuSO_4 - 2NO - 4H_2O$. The solution may be concentrated and allowed to crystallize or evaporated with frequent stirring, so that the salt will be obtained in the form of a coarse granular powder, which latter is more convenient for dispensing purposes.

The official crystallized cupric sulphate, containing 36.1 per cent. of water, slowly effloresces upon exposure to air; hence it must be kept in tightly closed vessels. When deprived of all of its water of crystallization at a temperature of 200° C. (392° F.), the anhydrous salt forms a valuable dehydrating agent and is used in the preservation of absolute alcohol.

Among the non-official compounds of copper the following may be mentioned as of interest to pharmacists:

COPPER ARSENITE. $CuHAsO_3$. This salt, which of late years has come somewhat into prominence, is obtained as a green precipitate by decomposing a solution of cupric sulphate with potassium arsenite.

COPPER ACETATE. $Cu(C_2H_3O_2)_2 - H_2O$. Crystallized cupric acetate, which was recognized in the Pharmacopœia of 1880, may be obtained by double decomposition of cupric sulphate and lead or calcium acetate; the solution after filtration is acidulated with acetic acid, concentrated and allowed to crystallize. This salt must not be confounded with ordinary verdigris, a basic cupric acetate, which occurs in amorphous masses and has the composition, $Cu_2O(C_2H_3O_2)_2$.

COPPER NITRATE. $Cu(NO_3)_2 - 3H_2O$. A very deliquescent salt recognized in the British Pharmacopœia and prepared from metallic copper by solution in diluted nitric acid and subsequent crystallization.

COPPER ALUM. By this name the German Pharmacopœia recognizes a mixture of alum, saltpetre, cupric sulphate, and camphor, which has also received the official Latin title, *cuprum aluminatum*. It is prepared by fusing together 16 parts each of potassium alum, cupric sulphate, and potassium nitrate, and adding to the fused mixture, after removal from the fire, 1 part each of powdered camphor and powdered potassium alum; after thorough incorporation of the powders the mass is poured out on a slab to solidify. This mixture is sometimes prescribed by physicians as *lapis divinus*.

The Compounds of Lead.

LEAD ACETATE. $Pb(C_2H_3O_2)_2 + 3H_2O$. This salt may be obtained by dissolving lead oxide in diluted acetic acid, or by exposing

lead in the form of sheets to the combined action of air and vinegar. The resulting solutions are filtered, concentrated, and crystallized; in order to secure perfect crystallization a little acetic acid is added to the liquid. Purified lead acetate for dispensing purposes is prepared in granular form by dissolving the large crystals in water, filtering and evaporating the solution with frequent stirring, so that small crystals may be produced.

Commercially, lead acetate is better known as sugar of lead, on account of its peculiar sweet taste. When exposed to the air it effloresces and slowly absorbs carbon dioxide; it must therefore be preserved in well-closed bottles or cans.

LEAD CARBONATE. $2PbCO_3+Pb(OH)_2$ or $Pb_3O(CO_3)_2$. As shown by the chemical formula, the official lead carbonate is not a normal carbonate, but a mixture of the same with lead hydroxide. It is obtained in various ways, known respectively as Dutch, German, French, and English methods, all of which have in view the preliminary preparation of basic lead acetate, which is then converted into basic carbonate by means of carbon dioxide.

Commercial lead carbonate, better known as white lead, occurs of variable composition, the proportion of lead hydroxide being much greater in some samples than in others. The Pharmacopœia demands the absence of more than 1 per cent. of insoluble foreign matter, such as sand and lead, barium and calcium sulphate; the yield of 85 per cent. of oxide upon strong ignition corresponds to a compound of the above composition.

Lead carbonate is the most poisonous of all lead compounds; hence, care must be observed in its application to excoriated surfaces. It is recognized in the German Pharmacopœia as Cerussa.

LEAD IODIDE. PbI_2. This salt is prepared by double decomposition between cold solutions of lead nitrate and potassium iodide; the precipitate is well washed with water and dried at a gentle heat. Lead acetate may be used in place of the nitrate, but entails a loss of the product, since lead iodide is appreciably soluble in potassium acetate solution.

Lead iodide may be adulterated with lead chromate, which resembles it in appearance; such an admixture can be detected by treatment with a hot solution of ammonium chloride, in which lead iodide is soluble, while lead chromate remains unaffected.

LEAD NITRATE. $Pb(NO_3)_2$. While metallic lead is soluble in diluted nitric acid, lead oxide or carbonate is preferred for the manufacture of this salt, as solution can be effected more readily; the solution of lead nitrate thus obtained is concentrated and crystallized. Lead nitrate is insoluble in alcohol, and in this respect differs from lead acetate, which is soluble in five times its weight of that liquid.

LEAD OXIDE. PbO. Of the different oxides of lead occurring on the market, only that more particularly known as litharge is officially recognized. It is obtained by heating lead in contact with air, to a temperature of about 400° or 450° C. (752° or 842° F.), and also as a by-product in the treatment of silver ores by the process known as cupellation.

When lead oxide is exposed to the air it slowly absorbs moisture and carbon dioxide, a basic lead carbonate being formed, hence it should be kept in well-closed vessels; the Pharmacopœia limits the increase in weight due to such absorption to 2 per cent. The color of commercial litharge is not uniform, which is due to the manner of cooling the molten mass; if allowed to cool slowly, a reddish-yellow product is obtained, while if cooled rapidly, a yellowish-red color results.

SOLUTION OF LEAD SUBACETATE. An aqueous liquid containing in solution about 25 per cent. of basic lead acetate of the approximate composition, $Pb_2O(C_2H_3O_2)_2$. The official directions for preparing this well-known solution are to boil for half an hour a mixture of 17 parts of lead acetate, 10 parts of lead oxide, and 80 parts of distilled water, supplying from time to time the water lost by evaporation, and finally adding to the cooled liquid enough boiled distilled water to bring the total weight up to 100 parts, after which the mixture is filtered.

The lead acetate should be dissolved in water first and the lead oxide then added in the form of a finely sifted powder; both compounds must be free from carbonate. Distilled water, preferably that which has been boiled, so as to avoid the presence of carbon dioxide, as well as sulphates and chlorides, should always be used in the preparation of this solution. The process of boiling the mixture is directed mainly for the purpose of economizing time, as the same changes will take place even at ordinary temperatures, several days, however, being required, together with frequent agitation of the vessel.

Several basic lead acetates are known, the composition of which depends upon the proportions in which the lead acetate and oxide are employed; thus the United States and British Pharmacopœias, using the acetate and oxide in the proportion of their molecular weights, obtain in solution the basic compound indicated by the formula, $Pb_2O(C_2H_3O_2)_2$, according to the equation, $(Pb(C_2H_3O_2)_2+3H_2O)+PbO=Pb_2O(C_2H_3O_2)_2+3H_2O$, while the German and French Pharmacopœias, directing the use of three parts of lead acetate to one of lead oxide, cause the production of a less basic compound, as shown by the equation, $2(Pb(C_2H_3O_2)_2+3H_2O)+PbO=Pb_3O(C_2H_3O_2)_4+6H_2O$.

In the preparation of this solution other basic lead acetates, such as $Pb_3O_2(C_2H_3O_2)_2$, are also formed in small quantities in addition to those already mentioned, and an insoluble white residue is always

left, consisting of a very basic compound, probably having the composition, $Pb_6O_5(C_2H_3O_2)_2$.

Solution of lead subacetate, commercially known as Goulard's Extract, is very sensitive to carbon dioxide, the least exposure to air causing a film of basic lead carbonate to form; hence it must be preserved in tightly stoppered bottles, and should always be filtered in a closely covered funnel. It is incompatible with solution of acacia, differing in this respect from the normal acetate.

The valuation of solution of lead subacetate is made by precipitation with normal sulphuric acid, lead sulphate being formed, according to the equation, $Pb_2O(C_2H_3O_2)_2+2H_2SO_4=2PbSO_4+2HC_2H_3O_2+H_2O$, which also shows that each Cc. $\frac{n}{1}H_2SO_4$ corresponds to 0.13662 Gm. of basic lead acetate of the approximate composition indicated by the Pharmacopœia. For 13.67 Gm. of the solution about 25 Cc. of normal acid will be required, as 25 per cent. of 13.67 is 3.4175, and $3.4175 \div 0.13662 = 25.01$. Methyl-orange has been selected as an indicator, since it can be used in the presence of free acetic acid (being unsuited for organic acids), which is not the case with litmus and some other color indicators; it causes a crimson color with sulphuric acid, and thus indicates the end reaction very sharply against the white background formed by the suspended lead sulphate.

The Pharmacopœia also recognizes a dilute solution of lead subacetate, made by mixing 3 volumes of the above solution with 97 volumes of distilled water. This preparation is popularly known as lead-water.

The Compounds of Zinc.

ZINC ACETATE. $Zn(C_2H_3O_2)_2+2H_2O$. This salt may be prepared by solution of either zinc oxide or carbonate in hot, moderately diluted acetic acid. After filtration the solution is allowed to cool, when a large portion of the newly formed salt separates. A further yield of crystals may be obtained by concentration of the mother-liquor. It is better to crystallize the salt from a slightly acid solution, so as to avoid the formation of basic zinc acetate.

Zinc acetate upon exposure to air slowly effloresces and loses acetic acid, a basic salt being formed at the same time; hence it should be preserved in well-stoppered bottles.

ZINC BROMIDE. $ZnBr_2$. The most convenient method for preparing this salt is digestion of pure granulated zinc with a solution of hydrobromic acid as long as reaction continues, then filtering and evaporating the solution to dryness. Zinc bromide may, however, also be obtained by mutual decomposition between zinc sulphate and potassium bromide or by the direct action of bromine on metallic zinc in the presence of water.

Zinc bromide is a very deliquescent salt, and must therefore be kept in bottles closed with glass stoppers coated with paraffin. The

Pharmacopœia requires absolute purity for this salt, allowing merely traces of moisture, which is determined by titration with decinormal silver nitrate solution. Since each molecule of dry zinc bromide requires two molecules of silver nitrate for complete precipitation, 0.3 Gm. will require 0.45289 Gm. of the silver salt; this quantity is represented by 26.71 Cc. of $\frac{N}{10}$ $AgNO_3$ solution.

Precipitated Zinc Carbonate. This compound is obtained by mutual decomposition between zinc sulphate and sodium carbonate. On mixing cold solutions of these two salts, normal zinc carbonate is precipitated in a gelatinous form, but rapidly undergoes decomposition, carbon dioxide being liberated, whereby a portion of the precipitate is again dissolved. If, however, the solution of zinc sulphate be added slowly and with constant stirring, to a boiling solution of sodium carbonate, carbon dioxide is rapidly expelled and a basic zinc carbonate precipitated, thus, $5(ZnSO_4 + 7H_2O) + 5(Na_2CO_3 + 10H_2O) = (2ZnCO_3 + 3Zn(OH)_2) + 5Na_2SO_4 + 3CO_2 + 82H_2O$; the mixture is boiled for a short time, after which the precipitate is washed with water until all sodium sulphate is removed and then dried at a gentle heat. Potassium carbonate is not so well adapted as the sodium salt for the process, as the resulting potassium sulphate is less readily washed out, and ammonium carbonate is unsuitable, since it does not completely precipitate the zinc.

The composition of commercial zinc carbonate will naturally vary with the particular process employed in its manufacture and the relative proportions of the two salts used. The British Pharmacopœia assigns the formula, $ZnCO_3 + 3Zn(OH)_2 + H_2O$, to the official article, thereby indicating a more basic compound than the one above mentioned.

Impure native zinc carbonate, contaminated with iron, is known in commerce as calamine, and was at one time used in pharmacy for the preparation of Turner's Cerate.

Zinc Chloride. $ZnCl_2$. This salt may be obtained by evaporating the official solution of zinc chloride to dryness, with constant stirring, adding toward the close of the operation a little hydrochloric acid to avoid, as far as possible, the formation of oxychloride. Owing to the very hygroscopic character of the salt, it must be transferred while still warm to perfectly dry bottles, which should be closed with paraffined glass stoppers.

The entire absence of basic salt in zinc chloride is scarcely possible, and the Pharmacopœia prescribes the limit by directing that 1 drop of hydrochloric acid shall clear up the opacity caused in 5 Cc. of a 5 per cent. aqueous solution of the salt by the addition of an equal volume of alcohol. If flocculi are observed in a solution of zinc chloride, they are evidence of the presence of oxychloride, and should be removed by the cautious addition of dilute hydrochloric acid. As zinc chloride acts destructively upon vegetable fibre, strong

solutions of it should always be filtered through asbestos or glass wool.

The Pharmacopœia demands that the official salt shall contain 99.84 per cent. of pure $ZnCl_2$; each Cc. of $\frac{N}{10}$ $AgNO_3$ solution corresponds to 0.006792 Gm. $ZnCl_2$, hence 0.3 Gm. of the salt will require 44.1 Cc. for complete precipitation, as 99.84 per cent. of 0.3 is 0.29952 and $44.1 \times 0.006792 = 0.29952$.

ZINC IODIDE. ZnI_2. This salt can be prepared by direct union of iodine and zinc in the presence of water, when zinc iodide will be formed with liberation of hydrogen. The solution thus obtained is evaporated, with constant stirring, to dryness, the resulting salt resembling zinc bromide in appearance. Upon exposure to air zinc iodide is gradually oxidized, iodine being liberated and the salt becoming colored, hence it must be kept in small, tightly stoppered vials; like the bromide it is also very deliquescent.

Zinc iodide should contain not less than 98.62 per cent. of pure ZnI_2, which is ascertained by titration with decinormal silver nitrate solution; each Cc. of the latter corresponds to 0.015908 Gm. ZnI_2, 0.5 Gm. of the official salt will require, therefore, not less than 31 Cc., for 98.62 per cent. of 0.5 is 0.4931, and $0.4931 \div 0.015908 = 31$. If 31.4 Cc. $\frac{N}{10}$ $AgNO_3$ solution be required for complete precipitation of 0.5 Gm. of zinc chloride, the salt is absolutely pure and dry, but if more be necessary, zinc bromide or chloride is present.

ZINC OXIDE. ZnO. For pharmaceutical purposes zinc oxide is usually obtained by heating precipitated zinc carbonate in a crucible until all carbon dioxide and water have been expelled, the process being identical with that for the production of magnesia; thus, $2ZnCO_3 + 3Zn(OH)_2 = 5ZnO + 2CO_2 + 3H_2O$. A red heat is not necessary, decomposition already taking place at a temperature of 250° or 280° C. (482° or 536° F.). The lower the temperature employed for expelling the carbon dioxide the whiter will be the oxide obtained, a full, red heat always causing a decided yellow tint.

Zinc oxide is occasionally designated as *flores zinci* (flowers of zinc), *nihil album* (white nothing), or *lana philosophica* (philosopher's wool), and an impure gray variety was formerly used under the name *tutia* or *tutty*.

ZINC PHOSPHIDE. Zn_3P_2. Phosphorus and zinc may be made to unite by carefully adding small pieces of the former to fused zinc contained in a crucible, but it is difficult to obtain a product of uniform composition. A more desirable method for preparing the compound is that of Proust, whereby a mixture of hydrogen phosphide and nitrogen is passed into a porcelain tube containing metallic zinc heated to redness, the metal combining with the phosphorus, while the nitrogen and liberated hydrogen escape together.

Zinc phosphide must be preserved in tightly stoppered vials, as,

upon exposure to air, it slowly emits phosphorous vapor, indicating decomposition and oxidation.

ZINC SULPHATE. $ZnSO_4+7H_2O$. This salt is manufactured on a large scale by digesting metallic zinc with diluted sulphuric acid, when zinc sulphate is formed and hydrogen eliminated. As iron is generally present in zinc, this also is dissolved and is removed by first converting it into a ferric salt (by passing chlorine into the solution) and afterward adding zinc carbonate, whereby all iron is precipitated as ferric hydroxide. The solution of zinc sulphate is separated by filtration, concentrated, and allowed to crystallize.

Commercial zinc sulphate frequently contains free acid, and is usually contaminated with iron and other metals; for pharmaceutical purposes only the purified salt in small crystalline granules should be used. On account of the acid reaction of an aqueous solution of zinc sulphate with litmus paper, free acid to be detected must be extracted with alcohol, which has no effect on the salt, as directed in the Pharmacopœia.

ZINC VALERIANATE. $Zn(C_5H_9O_2)_2+2H_2O$. When hot solutions of sodium valerianate and zinc sulphate are mixed double decomposition takes place, sodium sulphate and zinc valerianate being produced, the former of which remains in solution, while a portion of the zinc salt separates in the form of scaly crystals and rises to the surface; a further yield of crystals may be obtained upon concentration of the mother-liquor. The crystals are afterward drained, washed with small quantities of cold water, and dried at ordinary temperature.

SOLUTION OF ZINC CHLORIDE. An aqueous solution of zinc chloride, $ZnCl_2$, containing about 50 per cent. of the anhydrous salt. The official directions for preparing this solution are to digest metallic zinc with moderately diluted hydrochloric acid until the acid is saturated; the solution is decanted, and after the addition of a small quantity of nitric acid evaporated to dryness; the dry mass is next heated to fusion at a temperature not exceeding 115° C. (230° F.), allowed to cool and dissolved in sufficient water to bring the weight of the solution up to 1000 Gm. for every 840 Gm. of hydrochloric acid and 240 Gm. of zinc employed. Finally some zinc carbonate is added, the mixture agitated occasionally during 24 hours, allowed to settle, and the clear liquid decanted.

The object of adding nitric acid to the solution is to convert any iron present (derived from the zinc) into ferric chloride. To remove any nitrogen compounds or nitrate formed, the liquid is further evaporated to dryness and fused below 115° C. (230°. F.), so as to avoid volatilization of any zinc chloride. The final addition of zinc carbonate precipitates all iron as ferric hydroxide, and thus a solution of zinc chloride only is obtained.

Solution of zinc chloride has a specific gravity of about 1.535 at 15° C. (59° F.), and is chiefly used for disinfecting purposes. It is practically identical with Burnett's disinfecting fluid.

Besides the foregoing compounds of zinc the following are of interest:

ZINC HYPOPHOSPHITE. $Zn(H_2PO_2)_2+H_2O$. This salt may be conveniently prepared by dissolving zinc oxide or carbonate in hypophosphorous acid and allowing the solution to crystallize.

ZINC LACTATE. $Zn(C_3H_5O_2)_2+3H_2O$. If moderately dilute lactic acid be neutralized with zinc carbonate, heating the mixture if necessary, and the resulting solution concentrated and set aside to cool, crystals of the above composition will be obtained.

ZINC PHOSPHATE. $Zn_3(PO_4)_2+4H_2O$. When a hot solution of zinc sulphate is added to a hot solution of official sodium phosphate, a white crystalline precipitate of zinc phosphate results, which is subsequently washed with water to remove all sodium salt and then dried at ordinary temperature.

ZINC SALICYLATE. $Zn(C_7H_5O_3)_2+3H_2O$. This salt may be conveniently obtained by gradually adding to a hot mixture of the salicylic acid and water an aqueous suspension of zinc oxide as long as solution is effected, which is then filtered and allowed to crystallize.

ZINC SULPHOCARBOLATE. $Zn(SO_3C_6H_4OH)_2+8H_2O$. This salt may be prepared by mutual decomposition between solutions of barium or lead sulphocarbolate (see sodium sulphocarbolate) and zinc sulphate, filtering the mixture and evaporating the clear liquid to crystallization. The British Pharmacopœia recommends simple saturation of sulphocarbolic acid with zinc oxide. Crystals of zinc sulphocarbolate are of a reddish color unless the solution has been acidulated with sulphuric acid.

The Compounds of Gold.

GOLD AND SODIUM CHLORIDE. The official preparation is not the true double salt of the same name, but a mixture of gold chloride and sodium chloride. The double chloride of gold and sodium, known also as sodium chloroaurate, contains about 76 per cent. of pure auric chloride, whereas, the official compound contains but 50 per cent. The exact composition of commercial gold and sodium chloride depends upon the mode of preparation; a simple mechanical mixture made by triturating sodium and gold chlorides together

in equal proportions would be in conformity with the official definition, but if the preparation is made after the method directed in the German Pharmacopœia, a mixture of the true double salt and sodium chloride is sure to result; by adding a solution of sodium chloride to one of an equal weight of auric chloride and evaporating the mixture to dryness, a similar preparation is possibly obtained.

Anhydrous auric chloride, $AuCl_3$, may be prepared by dissolving gold in nitromuriatic acid, evaporating the solution to dryness, dissolving the residue in water, and carefully evaporating the liquid to dryness at a temperature not exceeding 150° C. (302° F.); this operation is necessary to free the salt from acid, but a higher temperature must be avoided, lest decomposition of the auric chloride into aurous chloride and chlorine occur.

A solution of metallic gold in a mixture of nitric and hydrochloric acids contains chloroauric acid, according to the equation, $Au_2+2HNO_3+8HCl=2HAuCl_4$ or $2(AuCl_3+HCl)+2NO+3H_2O$, and by adding to such a solution sodium chloride, the double salt, sodium chloroaurate, is obtained upon evaporation, thus: $HAuCl_4+NaCl=NaAuCl_4$ or $(AuCl_3+NaCl)+HCl$. For the formation of this compound 5.187 parts of auric chloride require 1 part of sodium chloride; hence, if equal parts of the two salts are used a large excess of the sodium chloride will be present.

The amount of gold present in any sample of the commercial double chloride can be ascertained by treatment with an excess of some reducing agent, whereby metallic gold is precipitated. Either ferrous sulphate or oxalic acid may be employed, the reaction occurring being illustrated by the following equations: $2AuCl_3+6(FeSO_4+7H_2O)=Au_2+2(Fe_2(SO_4)_3)+Fe_2Cl_6+42H_2O$ or $2AuCl_3+3(H_2C_2O_4+2H_2O)=Au_2+6CO_2+6HCl+6H_2O$. From the second equation it is seen that 377.1 parts of crystallized oxalic acid can precipitate 393.4 parts of metallic gold; hence, in the official test, 0.15 Gm. of the metal will require 0.143 Gm. of the acid, thus insuring the necessary excess of the latter.

Gold chloride being readily reduced by contact with organic matter, all such mixtures should be avoided, and as the official preparation is chiefly used in pill-form, non-oxidizable excipients only should be employed (see also page 313).

The Compounds of Silver.

Silver Cyanide. $AgCN$. This salt may be prepared either by passing freshly distilled hydrocyanic acid into a solution of silver nitrate or by adding a solution of the latter salt to a solution of pure potassium cyanide as long as a precipitate continues to be formed. In either case the precipitate must be well washed with water and dried in a dark place.

Silver cyanide becomes discolored upon exposure to light, and must

therefore be kept in dark bottles. It is used in pharmacy solely for the extemporaneous preparation of diluted hydrocyanic acid.

SILVER IODIDE. AgI. When a solution of silver nitrate is added slowly and with constant stirring to a solution of potassium iodide, a light-yellowish precipitate of silver iodide is formed by mutual decomposition, which, after being well washed with water, may be dried upon paper. Owing to the very slight solubility of silver iodide in ammonia water, contamination with silver chloride or bromide can be readily detected by the pharmacopœial tests. If absolutely pure the salt remains unaltered by exposure to light, but the commercial article usually assumes a greenish tint.

The salt is scarcely ever used in medicine now, and its recognition in the Pharmacopœia appears quite superfluous.

SILVER NITRATE. $AgNO_3$. This salt is preferably made from pure silver, and in order to obtain a product free from acid the metal is dissolved in nitric acid, the solution evaporated to dryness, the residue fused and redissolved in water, the solution filtered and allowed to crystallize. The evaporation to dryness and fusion of the residue are for the purpose of expelling any uncombined acid present, which, if the first solution were allowed to crystallize, would, to some extent, be mechanically retained within the crystals; a temperature exceeding 200° C. (392° F.) must, however, be avoided, lest some of the silver nitrate be reduced to nitrite.

Silver nitrate is easily decomposed by contact with organic matter, and when exposed to light gradually assumes a gray color; hence proper precautions must be observed in keeping and dispensing it.

The Pharmacopœia requires absolute purity for crystallized silver nitrate, which is determined by titration with decinormal sodium chloride solution. The equation, $AgNO_3+NaCl=AgCl+NaNO_3$, shows that 169.55 parts of the silver salt require 58.37 parts of sodium chloride for complete precipitation; hence each Cc. $\frac{N}{10}$ NaCl solution corresponds to 0.016955 Gm. $AgNO_3$, and 0.34 Gm. of crystallized silver nitrate requires 20 Cc. of the decinormal solution, for $0.016955 \times 20 = 0.33910$.

DILUTED SILVER NITRATE. This preparation differs from the preceding in containing only 33 1-3 per cent. of pure silver nitrate, and being much milder in its action, is also known as mitigated caustic. It is made by fusing together 30 parts of silver nitrate and 60 parts of potassium nitrate, and, when a smooth, uniform mixture results, pouring the molten mass into suitable moulds, usually of a narrow cone shape.

The amount of pure silver nitrate present in any sample may be ascertained by means of decinormal sodium chloride solution, an excess of which is added and determined subsequently by retitration with decinormal silver nitrate solution, using potassium chromate as

an indicator. The two solutions being of equal value volumetrically, the number of Cc. $\frac{n}{10}$ $AgNO_3$ solution required, after addition of 20 Cc. $\frac{n}{10}$ NaCl solution in the official test, to cause a permanent red precipitate of silver chromate, subtracted from 20 gives the exact number of Cc. $\frac{n}{10}$ NaCl solution necessary to precipitate all the silver from 1 Gm. of diluted silver nitrate; this number multiplied by 0.016955 and then by 100 gives the percentage of silver nitrate present in the sample.

MOULDED SILVER NITRATE. Under this name the Pharmacopœia recognizes a mixture of silver nitrate and chloride, containing 5 per cent. of the latter salt, and prepared by adding 1 part of hydrochloric acid to 25 parts of pure silver nitrate, melting the mixture at as low a temperature as possible and casting the mass in moulds. The object of converting a part of the silver nitrate into chloride is to render the resulting mass less brittle.

The synonym, *lunar caustic*, given to this preparation in the Pharmacopœia does not correspond with the same term commercially, which is usually applied to pure silver nitrate moulded into sticks, as also indicated in the British Pharmacopœia. The latter authority applies the name *toughened caustic* to a mixture of 95 parts of silver nitrate and 5 parts of potassium nitrate.

The valuation of fused silver nitrate is made exactly as in the case of diluted silver nitrate. Like all silver salts, this one must also be protected from light to prevent discoloration.

SILVER OXIDE. Ag_2O. This compound may be obtained by adding a solution of pure silver nitrate to a solution of potassa, soda, or lime, washing the resulting precipitate well with water and finally drying the same on a water-bath. Ammonia water is not suitable for the process, since it forms a soluble compound with the oxide, having the composition Ag_2O+NH_3.

When ignited in a porcelain crucible, silver oxide should yield 93.1 per cent. of its weight of metallic silver. Like silver iodide, the oxide is very rarely employed in medicine at the present time. It is quickly decomposed by oxidizing agents, and must never be triturated with organic substances.

ORGANIC SUBSTANCES.

UNDER this head are classified those many compounds of carbon, hydrogen, and oxygen, frequently associated with nitrogen, sulphur, phosphorus, and other elements, which are chiefly derived from the vegetable kingdom; a few are also obtained from the animal kingdom, and some are produced synthetically.

Prior to 1828, when Woehler announced to the scientific world the successful synthetic production of urea, an excretory product of the animal economy, solely from inorganic material, thereby establishing the intimate relationship between organic and inorganic matter, the agency of a peculiar vitalizing force was considered essential for the formation of all so-called organic bodies. No elements unknown to the mineral kingdom have ever been found in organic bodies, and the one feature which serves to distinguish this very large class of chemical compounds from those commonly designated as inorganic substances, is the invariable presence of carbon; the term carbon compounds is therefore most appropriately applied to them.

The simplest form of carbon compounds are the hydrocarbons, composed exclusively of carbon and hydrogen; of these, two, methane, CH_4, and benzene, C_6H_6, may be said to be the source of all organic compounds, the constitution of which has thus far been studied and explained. The derivatives of these two hydrocarbons differ so widely in their properties that they have been conveniently grouped into two main classes, designated as fatty and aromatic compounds respectively.

It is not within the scope of this book to enter into a detailed study of the so-called organic substances, and attention will be given only to those of pharmaceutical interest.

CHAPTER LII.

CELLULOSE AND ITS DERIVATIVES.

ALL plants are made up of certain proximate principles, to which they owe their growth and value as nourishing or medicinal agents. The most widely diffused substance in the vegetable kingdom is cellulose or cell membrane, which goes to make up the body of all plants. During the growth and development of plants, some of the cell membrane undergoes a change, becoming gradually hard and woody; to this modified form of cellulose the name lignin has been given, and the woody fibre of plants is assumed to be a combination of cellulose and lignin, called lignose. Cellulose and lignin being insoluble in all ordinary solvents, the chief object in pharmaceutical processes is to extract from them, by appropriate treatment, the many valuable principles they often enclose and upon which the medicinal value of vegetable drugs depends.

Lignin has not yet been obtained in a pure state, but pure cellulose has been isolated as a colorless, odorless, and tasteless gelatinous mass, which, upon drying, forms a horny substance, or may be obtained as a white powder. It is soluble in a solution of cupric hydroxide in ammonia water, known as Schweitzer's reagent, forming a mucilaginous fluid which, after dilution, admits of filtration, and, upon addition of an acid, is again precipitated. The elementary composition of pure cellulose corresponds to the formula, $C_6H_{10}O_5$, or multiples thereof, as $C_{12}H_{20}O_{10}$ or $C_{18}H_{30}O_{15}$.

Cellulose is officially recognized in the form of gossypium, or cotton, and patent lint and paper are further examples of it. When heated with potassium or sodium hydroxide it is gradually converted into oxalic acid, alkali oxalates being formed, and, if boiled with diluted sulphuric acid, dextrin is produced, which is finally changed into dextrose, from which alcohol can be obtained by fermentation. Immersed in strong sulphuric acid, cellulose undergoes conversion into a substance called amyloid, upon which the preparation of parchment paper depends, the pores of the paper becoming filled with this modified cellulose, and thus made tough and impervious to water. Prolonged contact of the paper with strong sulphuric acid, however, is hurtful, the resulting product becoming friable; hence the best results are obtained if the paper be simply drawn through a mixture of two parts of concentrated sulphuric acid and one part of water, and then immediately well washed in water.

Official purified cotton, commercially better known as absorbent

cotton, is prepared by first boiling carefully carded cotton in a weak alkaline solution, for the purpose of removing fatty matter, after which it is rinsed in water and immersed in a weak solution of chlorinated lime. It is subsequently washed in water slightly acidulated with hydrochloric acid and again well rinsed in water. If the cotton still retains fat, the treatment with alkali is repeated until the final product is found completely absorbent. For the more thorough removal of water after washing the cotton, recourse is had to centrifugal machines by means of which the material is rapidly dried.

Medicated cotton is usually prepared by impregnating absorbent cotton with a solution of the medicinal agent in alcohol and glycerin and subsequently drying; the glycerin not being volatilized serves as an adhesive agent for retaining the active ingredient on the fibre of the cotton. The solution is used of a definite strength and in such quantity that the whole of it will be absorbed by and saturate the material. Benzoated, borated, carbolated, iodized, salicylated, and other medicated cotton is prepared in this or a similar manner. The percentage of medicinal agent present must be calculated on the basis of finished product, irrespective of any adhesive agent that may have been employed, and which naturally forms a part of the finished product; thus, 25 Gm. of 10 per cent. borated cotton should contain 2.5 Gm. of boric acid or 10 Gm. of 5 per cent. carbolated cotton should contain 0.5 Gm. of pure carbolic acid, etc. It has been suggested that impregnation of cotton with a 5 or 10 per cent. solution of any medicinal agent would constitute such cotton a 5 or 10 per cent. medication; but such an assumption is erroneous, since the absolute quantity of medicinal agent retained by the cotton must always be uncertain and variable in its relation to the weight of the finished product.

Cellulose and lignose both furnish most valuable pharmaceutical derivative products, the former by appropriate treatment with nitric acid and the latter by dry distillation.

PYROXYLIN. Under this name the United States and British Pharmacopœias recognize a compound soluble in a mixture of alcohol and ether, and better known as collodion cotton, since it is used extensively in the preparation of collodion; the name colloxylin is also used as a synonym in this country. In Continental Europe the two terms are not considered synonymous, the name pyroxylin being applied to insoluble gun-cotton, and colloxylin to the soluble collodion cotton. Pyroxylin is officially prepared by macerating purified cotton in a cooled mixture of 14 volumes of nitric acid and 22 volumes of sulphuric acid until the cotton has become soluble in a mixture of 1 volume of alcohol and 3 volumes of ether, then removing all adhering acid by washing first with cold and then with boiling water and finally drying the product in small portions at a moderate heat (60° C. (140° F.)).

When cotton is thoroughly imbued with strong nitric acid, cellu-

lose nitrates and water are formed; thus, $C_6H_{10}O_5 + 2HNO_3 = C_6H_8(NO_3)_2O_3 + 2H_2O$. The exact character of the reaction depends upon the strength of the acid used, the temperature at which the cotton is immersed, and the length of time maceration is continued; thus, di-, tri-, tetra-, penta-, and hexanitrate may be produced. The last two compounds are insoluble in alcohol and ether, and hence unfit for the purposes of official pyroxylin, which latter probably consists of a mixture of cellulose di- and trinitrate. It is important that the acids used be of official strength, and that the acid mixture, which becomes heated, be allowed to cool down to 32° C. (90° F.) before the cotton is added, otherwise, in the latter case, the higher nitrates are formed and the staple of the cotton is destroyed; if weak acids be employed, prolonged maceration becomes necessary and imperfect nitration may result; in either case the product is insoluble.

In order that the cotton may be completely saturated with the acid mixture, it should be introduced in small portions, by the aid of a glass rod. The sulphuric acid used takes no part in the reaction, but facilitates the same by removing the water which is eliminated.

Pyroxylin was at one time looked upon as a nitro substitution compound, and called nitrocellulose, the group NO_2 having been supposed to replace hydrogen in cellulose. Further studies of cellulose and the behavior of pyroxylin toward reagents have shown the latter compound to be a nitric acid ester or compound ether, formed by the displacement of hydrogen in the hydroxyl groups by the nitric acid radical, as shown by the formulas, $C_6H_8(ONO_2)_2O_3$ or $C_6H_7(ONO_2)_3O_2$. The correctness of this view is shown by the fact that nitric acid can be abstracted from cellulose nitrates by treatment with alkalies, and can also be completely displaced by concentrated sulphuric acid, even in the cold. All cellulose nitrates can be converted back into cellulose by reducing agents, and the degree of nitration can be definitely determined by treatment with ferrous sulphate and hydrochloric acid, the nitric oxide liberated being collected in a graduated tube, and from this the amount of nitric acid present can be calculated; the following equation explains the reaction: $2C_6H_7(ONO_2)_3O_2 + 18HCl + 18FeSO_4 = 2C_6H_{10}O_5 + 6NO + 6Fe_2(SO_4)_3 + 3Fe_2Cl_6 + 6H_2O$.

Pyroxylin is used in pharmacy exclusively in the preparation of plain and medicated collodion (see page 284), but has met with more extensive application in the arts in the manufacture of celluloid, a mixture of pyroxylin and camphor.

THE PRODUCTS OF DISTILLATION. When wood is subjected to heat in air-tight cylinders or retorts a number of new substances are obtained, as a result of destructive distillation, the character of which depends largely upon the degree of heat employed and the care with which the process has been conducted. Both liquid and gaseous products are formed and distil over, while the solid residue is either charcoal or the original wood employed, but slightly altered in

appearance. The liquid distillates include an acid fluid and tar; the former is known as pyroligneous acid or wood vinegar, which contains, besides acetic acid, acetone, C_3H_6O, methyl or wood alcohol, CH_3OH, furfurol, $C_5H_4O_2$, catechol or pyrocatechin, $C_6H_4(OH)_2$, and other substances.

Acetic Acid. Although this acid can be produced by the oxidation of weak alcoholic liquids, it is obtained for the trade by distillation of wood. In order to avoid, as far as possible, contamination with empyreumatic products, the distillation is carried on at a temperature below that at which the formation of charcoal occurs, or below 220° C. (428° F.). At the extensive acetic acid works of E. R. Squibb & Sons, in Brooklyn, N. Y., oak wood cut into small pieces, about four inches in length, is fed into large rectangular iron retorts, which are then heated in appropriate furnaces and kept at a temperature of 205° C. (401° F.) for a period of seven days, during which time a slightly colored liquid, dilute crude acetic acid, distils over, the wood losing about one-half in weight and assuming a dark walnut color and slight empyreumatic odor, but retaining its original structure and elementary composition. The acid liquid is neutralized with soda ash or sodium carbonate, and the resulting sodium acetate, having been obtained dry by evaporation, is roasted on top of the furnaces heating the retorts, whereby empyreumatic products are destroyed and water and other volatile matter driven off. Upon treating the sodium acetate with sulphuric acid, in suitable stills, purified acetic acid is recovered.

If wood is distilled at temperatures above 230° C. (446° F.), the resulting wood vinegar is more or less highly colored and possesses a strong empyreumatic odor. It requires a more tedious process of purification by means of milk of lime, whereby soluble calcium acetate is formed and many impurities are precipitated as insoluble calcium compounds; the calcium acetate can be converted into sodium acetate by treatment with sodium sulphate, which is then further purified by solution, recrystallization, roasting, etc., and is finally decomposed by distillation with sulphuric acid.

Chemically, acetic acid may be looked upon as methane or marsh-gas (CH_4), in which an atom of hydrogen has been replaced by the carboxyl group, CO_2H, forming a monobasic acid, thus: $CH_3CO_2H = HC_2H_3O_2$. It is a remarkably stable acid, and, although rich in oxygen, is not decomposed at moderately high temperatures, nor is it readily affected by oxidizing or reducing agents.

The Pharmacopœia recognizes three grades of acetic acid, which are officially designated as glacial acetic acid, acetic acid, and diluted acetic acid, and contain, respectively, 99, 36, and 6 per cent. of absolute $HC_2H_3O_2$. The three acids, recognized by the same names in the British Pharmacopœia, correspond very closely in strength to the above, containing 99, 33, and 4.27 per cent. of absolute acetic acid respectively; but in the German Pharmacopœia the term

acetic acid is used to designate a solution containing 96 per cent. of absolute acid, while the German diluted acetic acid contains 30 per cent.

Specific gravity is of no value in the examination of acetic acid, since the maximum density is reached in an 80 per cent. solution; beyond this point the specific gravity again decreases until absolute acetic acid is reached, having a density of 1.053. Official glacial acetic acid and an acid of 46 per cent. have the same specific gravity, 1.058, at 15° C. (59° F.), and, if diluted with water, the density of the weaker acid only will fall, that of the stronger acid increasing; between 73 and 84 per cent. acetic acid the specific gravity is almost stationary, the rise between these two points amounting to not more than 8 ten thousandths. Titration with normal alkali solution, as directed in the Pharmacopœia, is the only correct means of ascertaining the strength of acetic acid solutions, each Cc. of $\frac{N}{1}$ KOH solution corresponding to 0.05986 Gm. of absolute $HC_2H_3O_2$, as shown by the equation, $KOH + HC_2H_3O_2 = KC_2H_3O_2 + H_2O$.

Glacial acetic acid is obtained by distilling anhydrous sodium acetate with highly concentrated sulphuric acid and exposing the resulting liquid to a temperature below 10° C. (50° F.); after crystallization has taken place, the remaining liquid may be drained off and again exposed to cold to secure a further yield of crystals. Glacial acetic acid of official strength should retain its crystalline form at least until a temperature of 15° C. (59° F.) is reached, when it slowly begins to liquefy; much of the so-called glacial acetic acid of commerce is simply a strong solution, containing from 75 to 85 per cent. of absolute acid and does not solidify at a temperature of 5° C. (41° F.) or even lower.

The Pharmacopœia directs the use of glacial acetic acid in the preparation of solution of ferric acetate, and it is also employed as an excellent solvent for certain essential oils, resins, and fatty bodies. The acid absorbs moisture from the air, and must therefore be preserved in tightly-stoppered bottles.

Official acetic acid is obtained, like the glacial acid, by distilling sodium acetate with sulphuric acid and finally adjusting the strength to the requirements of the Pharmacopœia. It should contain 36 per cent. of absolute acetic acid, and is used in pharmacy chiefly for the preparation of the official diluted acid, and also as an addition to the menstruum employed for tincture of sanguinaria and several fluid and solid extracts.

Acetic acid for pharmaceutical purposes should be free from empyreuma, which may be detected by means of potassium permanganate, the color of which is readily discharged by empyreumatic substances. Upon neutralizing the acid with alkali and warming no foreign odor should be perceptible.

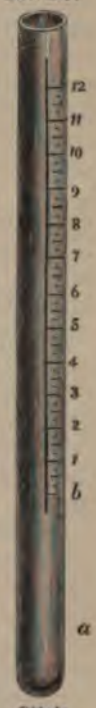
Pharmacists will find it to their interest to purchase strong acetic acid and dilute this to suit their requirements, according to the rule given on page 65. Acetic acid of 60 and 80 per cent. strength can

be purchased from reliable manufacturers at relatively lower prices than the official acid.

During the past few years many experiments have been made with the view of utilizing a strong (60 per cent.) acetic acid in place of alcohol for the extraction of aromatic, alkaloidal, and resinous principles from vegetable drugs. The results thus far obtained have been very encouraging, and manufacturers have already successfully applied this new menstruum in the preparation of certain aromatic solutions.

As the Pharmacopœia requires the official acetic acid to contain 36 per cent. of absolute $HC_2H_3O_2$, each gramme of the acid will neutralize exactly 6 Cc. of normal potassium hydroxide solution. The commercial variety of acetic acid known as "No. 8" should never be used in place of the official acid, as it is weaker, containing only 30 per cent. of absolute acid.

FIG. 280.



Otto's acetometer.

Diluted acetic acid, recommended in the Pharmacopœia in place of commercial vinegar as a menstruum for several official preparations, is made by mixing 100 Gm. of the 36 per cent. acid with 500 Gm. of water, and contains, therefore, 6 per cent. of absolute $HC_2H_3O_2$. Its advantages over ordinary vinegar are purity and uniformity of strength, besides which the entire absence of color enables it to be used for colorless solutions, such as spirit of Mindererus and the like.

While titration with normal alkali solution is always to be preferred as a means of ascertaining the strength of dilute solutions of acetic acid, other methods are also employed, such as neutralization with sodium or potassium bicarbonate, or with a standard ammonia solution, in an instrument known as Otto's acetometer, see Fig. 280. The latter method is largely used in vinegar establishments and gives results accurate to within one-fifth of one per cent. The acetometer consists of a graduated glass cylinder with rounded bottom, 36 centimeters (14.4 inches) in length and 3 centimeters (0.8 inch) internal diameter. The lower two graduations, marked *a* and *b*, indicate a volume of 1 and 10 Cc. respectively, while the upper part, from *b* to 12, is divided into 48 spaces each equivalent to 0.52 Cc., hence the large space between any two figures represents 2.08 Cc. The solution of ammonia used for the test contains 1.4 per cent. of absolute NH_3, and is prepared by mixing 14 Gm. of official 10 per cent. ammonia water with 86 Gm. of distilled water; every 2.07 Gm. of the solution measure 2.08 Cc. and correspond to 0.1 Gm. of absolute $HC_2H_3O_2$. When vinegar is to be tested, 1 Cc. of litmus test-solution is first poured into the tube, 10 Cc. of vinegar are then added, whereby the color of the litmus solution is changed to red, and finally sufficient of the above mentioned ammonia solution until, with gentle agitation, the blue color of the liquid is

restored. From the volume of ammonia solution used, as shown by the graduated cylinder, the amount of absolute acetic acid present can be readily calculated.

When chlorine is allowed to act on acetic acid in the sunlight, chloracetic acid is formed, three varieties of which are known, the most important being trichloracetic acid, $HC_2Cl_3O_2$. This latter compound occurs in deliquescent crystals, and is obtained by treating chloral hydrate with fuming nitric acid, exposing the mixture to sunlight for several days until red fumes are no longer evolved and then distilling.

Among the substances associated with acetic acid in crude wood vinegar are two of greater interest to pharmacists than the rest—acetone and methyl alcohol. Acetone, C_3H_6O or CH_3COCH_3, also known as pyroacetic spirit, was heretofore obtained on a commercial scale solely by the destructive distillation of acetates (chiefly calcium acetate), but recently (1895) a process has been devised by Dr. E. R. Squibb for decomposing acetic acid vapor at a high temperature, between 500° and 600° C. (932° and 1112° F.), in a specially constructed iron rotary apparatus, whereby a large yield of fairly pure acetone may be secured. The crude acetone thus obtained is afterward purified by dehydration with caustic lime and redistillation. The decomposition of acetic acid vapor results in the formation of acetone and carbon dioxide with the liberation of water, thus: $2HC_2H_3O_2 = C_3H_6O + CO_2 + H_2O$. The process and apparatus are fully described in *Ephemeris*, vol. iv., No. 3.

Chemically, acetone belongs to the class of compounds known as ketones, which consist of two alcohol radicals united by means of the bivalent group CO, called carbonyl; hence acetone is also called dimethyl ketone, and may be looked upon as acetic aldehyde, CH_3COH, in which the hydrogen atom is replaced by the methyl group.

Acetone is now extensively employed for the manufacture of chloroform, and has been found a valuable solvent for oleoresins, collodion cotton, etc. When pure it is a colorless, mobile, inflammable liquid of 0.7966 specific gravity at 15° C. (59° F.), and boiling at 56.3° C. (133.34° F.). It is miscible in all proportions with water and alcohol, hence the commercial article is usually contaminated with these substances.

Methyl alcohol, or wood alcohol, CH_3OH, also known as pyroxylic spirit, or wood naphtha, boiling at a comparatively low temperature—66° C. (150.8° F.)—may be obtained in a crude state by distilling wood vinegar after neutralizing with sodium carbonate or lime, and collecting the first portions coming over; wood vinegar usually contains about 10 per cent. of wood alcohol. It is purified by heating in a water-bath, with an excess of anhydrous calcium chloride, with which methyl alcohol forms a crystalline compound, $CaCl_2 + 4CH_3OH$, and, after all volatile matter has been dissipated, mixing the crystals with water and distilling, whereby the compound

is split up and dilute methyl alcohol recovered, which is subsequently dehydrated with lime and redistilled. Methyl alcohol has been used in England and Germany for the purpose of rendering ordinary or ethyl alcohol unfit for other than technical uses, by mixing the two liquids together; in Germany a further addition of allyl alcohol and acetone is prescribed. Ethyl alcohol thus mixed is known in England as methylated spirit, and in Germany as denaturated alcohol; it is not subject to excise tax.

TAR AND ITS DERIVATIVES. Like wood vinegar, tar is a complex mixture containing different resins, oils, hydrocarbons, phenols, etc., and yields valuable medicinal products. Official tar is derived from pine wood, and is recognized in the Pharmacopœia as Pix Liquida, or liquid pitch; by distillation it yields the official oil of tar and a hard residue known as black pitch.

The most valuable derivative of wood tar is creosote, a mixture of phenol-like bodies consisting chiefly of guaiacol and creosol. Beechwood tar is richer in creosote than that derived from other woods, containing usually about 5 per cent., and is therefore a more economical source. Upon distilling the tar, a light and a heavy oily layer are obtained, together with an acid aqueous distillate; the heavy oil is subsequently treated with a concentrated solution of sodium carbonate, to remove acid constituents, and again distilled. That portion of the second distillate heavier than water, and consisting of impure creosote, is dissolved in a moderately strong solution of potassa or soda; any oily layer separating is removed, and the creosote precipitated by saturating the alkaline solution with sulphuric acid. The alternate treatment with alkali and acid is repeated until the alkaline solution is practically free from color and does not turn brown on heating. The precipitated creosote is finally washed with a weak alkaline solution and water, and distilled, that portion distilling between 200° and 220° C. (392°–428° F.) being collected.

As wood vinegar also contains small proportions of creosote, the latter is recovered therefrom by first separating the oily constituents by saturating the liquid with sodium sulphate, treating these with sodium carbonate solution, distilling, and proceeding further as above.

When first distilled, creosote is colorless, but gradually assumes a yellowish tint, and, as found in commerce, is rarely free from color; upon exposure to air the color darkens materially. Much of the commercial creosote is coal-tar creosote or partially rectified carbolic acid, consisting largely of cresols, and is totally unfit for medicinal use; for dispensing purposes only the official beechwood creosote should be employed, which may readily be distinguished from carbolic acid by its peculiar odor, its lesser solubility in water, and its immiscibility with a mixture of glycerin and water.

The name creosote was given to this liquid on account of its power of preserving meat, and is derived from two Greek words—*κρεας*,

flesh, and σωζειν, to save, to preserve. Creosote was first separated from wood tar in 1832.

Whenever creosote is to be dispensed in solution in plain water or lime water the resulting mixture should invariably be passed through a pledget of cotton, as small particles of insoluble matter frequently separate, particularly in the case of lime-water mixtures.

Of late years creosote has been largely superseded by guaiacol, its chief constituent, upon which the value of creosote no doubt wholly depends. Guaiacol is contained in creosote to the extent of from 60 to 90 per cent., and is obtained from it by fractional distillation, that portion distilling between 200° and 205° C. (392° and 401° F.) being collected as crude guaiacol; this is treated with ammonia to remove acid compounds, and again distilled. The lower boiling fraction is collected, dissolved in ether, and treated with alcoholic solution of potassa, which causes the separation of potassium-guaiacol, $C_6H_4KOCH_3$, the latter being insoluble in ether. After thorough washing with ether the compound is crystallized from alcohol, decomposed by means of diluted sulphuric acid, and the liberated guaiacol again rectified. Guaiacol is rarely found absolutely pure in commerce, but can be obtained by treating pure benzoylguaiacol with alcoholic solution of potassa, and subsequently washing and rectifying the product; among chemists guaiacol is also known as methylcatechol, being the methyl ether of catechol (pyrocatechin), $C_6H_4(OH)OCH_3$. (A more complete account of the properties and various combinations of guaiacol may be found in the National Dispensatory, 5th ed., p. 799.)

CHAPTER LIII.

THE DERIVATIVES OF COAL TAR.

DURING the destructive distillation of coal, itself a modified form of wood, the result of slow decomposition caused by decay and fermentative action, gaseous as well as liquid products are obtained, besides a solid residue known as coke, the process being similar to that occurring in the distillation of wood. The gases are used extensively for illuminating and heating purposes, while the coal tar which contains benzene, C_6H_6, toluene, C_7H_8, aniline, $C_6H_5NH_2$, naphtalene, $C_{10}H_8$, carbolic acid, C_6H_5OH, and other important substances, is further distilled and furnishes, besides a solid residue, known as pitch or asphalt, a light and a heavy oil from which the above compounds are extracted.

The distillate of coal tar known as light oil consists chiefly of hydrocarbons of various boiling points, which can be separated from each other by fractional distillation. The most important of these is benzene, C_6H_6, designated by many as benzol, which furnishes a number of valuable derivative products; it is obtained by collecting that portion of light oil distilling between 80° and 90° C. (176° and 194° F.), purifying the same by exposing it to a low temperature, when it crystallizes and is freed from adhering liquid impurities and redistilling. Benzene has a specific gravity of 0.880 at 15° C. (59° F.), and is soluble in four parts of alcohol; it must not be confounded with benzin, a mixture of hydrocarbons obtained by distillation from coal oil or petroleum. The latter substance is recognized in the Pharmacopœia and is also known as petroleum ether; it has a specific gravity of about 0.670 at 15° C. (59° F.), boils between 50° and 60° C. (122° and 140° F.), and requires not less than six parts of alcohol for solution. Both liquids are readily inflammable and must be preserved with care; they have been found valuable solvents for fats, resins, caoutchouc, volatile oils, and some alkaloids, and are used in plant analysis.

Benzene is extensively employed in the manufacture of aniline, which in turn is used for the preparation of certain valuable pharmaceutical products, such as acetanilid, antipyrine, etc. When benzene is added in small portions to warm, fuming, nitric acid, a dark red liquid is formed, from which, upon the addition of water, an oily precipitate is obtained, known as nitrobenzene, $C_6H_5NO_2$.

By the action of nascent hydrogen, subsequent mixture with milk of lime and distillation, nitrobenzene is made to yield a basic fluid, called aniline. It has the composition $C_6H_5NH_2$, and is also known

as amidobenzene or phenylamine; when pure and recently obtained, it is a colorless oily liquid, but darkens upon exposure to air.

ACETANILID. $C_6H_5NHC_2H_3O$. The only derivative of aniline recognized in the Pharmacopœia is acetanilid, also known as phenylacetamide. The term anilid is applied to a class of compounds derived from aniline by replacement of one or both hydrogen atoms of the amido group, NH_2, by alcohol or acid radicals, hence both alcohol and acid anilids are known to chemists. Acetanilid is prepared by heating in a flask connected with a reflux condenser, a mixture of equal parts of aniline and glacial acetic acid, until a small portion of the mixture removed from the flask congeals on cooling; the mass is then distilled, when water and acetic acid first pass over, and afterward acetanilid, which is subsequently recrystallized from boiling water. The reaction involved in this process consists in the formation of aniline acetate, which, upon heating, is split up into acetanilid and water, as shown by the equation, $C_6H_5NH_2+HC_2H_3O_2=C_6H_5NHC_2H_3O+H_2O$.

The name antifebrin has also been given to acetanilid, but being a proprietary name has not been officially accepted as a synonym in most countries, although it is recognized in the Austrian Pharmacopœia. A compound closely allied to acetanilid is commercially known as *exalgine;* it is methylacetanilid, $C_6H_5NCH_3C_2H_3O$, and differs from acetanilid in having both hydrogen atoms of the amido group replaced, one by an alcohol radical, the other by an acid radical.

Antipyrine is also prepared from aniline by a complicated process. It has not been introduced into the United States Pharmacopœia, but is recognized in the German and British Pharmacopœias, being designated as Phenazone by the latter authority. Antipyrine is a well-characterized base and forms salts with acids by direct addition. Its constitution is indicated by its chemical name, dimethylphenylpyrazolon, but the copyrighted name, antipyrine, is usually employed by physicians and in commerce; such names as analgesine, methozine, anodynine, and parodyne have also been used as synonyms. Antipyrine is not used so freely now as formerly, and has been found to be incompatible with numerous drugs, such as sodium bicarbonate and salicylate in solid form, chloral hydrate, spirit of nitrous ether, tinctures containing tannin, etc.

RESORCIN. $C_6H_4(OH)_2$. Another derivative of benzene used in medicine is resorcin. Although first discovered by fusion of certain resins, as those of ammoniac, galbanum, guaiacum, asafetida, etc., with potassa, it is now manufactured on a large scale from benzene by first heating the latter with fuming sulphuric acid to 275° C. (527° F.), whereby benzene metadisulphonic acid, $C_6H_4(HSO_3)_2$, is formed. This acid is neutralized with milk of lime, decomposed with sodium carbonate, and the solution of sodium benzene-metadisulphonate thus obtained evaporated to dryness; the residue fused for several hours with sodium

hydroxide yields sodium resorcin and sodium sulphite. Boiling an aqueous solution of the saline mass expels sulphurous acid and, upon extracting the tar-like residue with ether and distilling, impure resorcin is obtained, which is purified by sublimation and recrystallization from water.

Resorcin is chemically known as metadioxybenzene, which shows it to be a diatomic phenol, $C_6H_4(OH)_2$; two isomerides are also known, namely, ortho-and paradioxybenzene, designated as catechol or pyrocatechin and hydroquinol or hydroquinone respectively. The term resorcinol is given as a synonym in the Pharmacopœia, but this name has also been applied to a proprietary preparation composed of equal parts of resorcin and iodoform fused together, hence confusion is apt to arise.

Pure resorcin occurs in colorless crystals, which readily assume a pink tint, and finally turn red upon exposure to air and light; it must, therefore, be carefully preserved, in tightly-stoppered bottles, in a dark place. Solutions of resorcin also become rapidly colored, hence should always be dispensed in dark amber-colored vials.

CARBOLIC ACID. C_6H_5OH. This substance is chiefly met with in the heavy oil distilled from coal tar, better known as dead oil. Crude carbolic acid, which is also recognized in the Pharmacopœia, is obtained by collecting that portion of dead oil distilling between 150° and 200° C. (302° and 392° F.) and twice redistilling the same between 160° and 190° C. (320° and 374° F.). It may be purified by agitating with warm solution of soda, whereby crystalline sodium phenol, C_6H_5ONa, is produced, which is freed from accompanying foreign matter by heating and treating with water; the aqueous solution is finally supersaturated with hydrochloric acid, precipitating the phenol as an oily liquid. This is repeatedly shaken with sodium chloride solution, dehydrated with calcium chloride and distilled between 165° and 185° C. (329° and 365° F.). Upon exposing the distillate to a low temperature, it solidifies into a crystalline mass.

Some manufacturers simply separate the pure carbolic acid from the crude by fractional distillation, carefully collecting that portion passing over between 165° and 185° C. and allowing it to crystallize.

The Pharmacopœia requires that carbolic acid shall contain not less than 96 per cent. of pure phenol and have a congealing point not lower than 35° C. (95° F.) and a boiling point not higher than 188° C. (370.4° F.). Absolutely pure carbolic acid melts at about 41° C. (105° F.) and boils at 178° C. (350.4° F.), hence the higher the melting point and the lower the boiling point the purer is the acid.

Of late years synthetic carbolic acid has been offered for sale. It is remarkably free from foreign matter, and is obtained by treating benzene with sulphuric acid, whereby benzenesulphonic acid,

$HSO_3C_6H_5$, is produced, which is then converted into sodium or potassium benzenesulphonate; this latter compound, upon being fused with an excess of alkali, is converted into alkali carbolate and sulphite, the former of which, upon addition of hydrochloric acid, splits up into alkali chloride and carbolic acid. Final distillation of the carbolic acid yields a pure product.

Several varieties of carbolic acid of American, English, German, and French manufacture occur on the market. For dispensing purposes only the crystallized acid should be used, which can be liquefied on a water-bath and retained in liquid form by addition of 10 per per cent. of distilled water. Calvert's carbolic acid No. 1, an English preparation, is of very fine quality and probably more extensively used in this country than any other variety. For disinfecting purposes, different kinds of crude carbolic acid, varying from a very dark almost black, to a nearly colorless solution, are employed; they consist chiefly of cresols, C_7H_7OH, with varying proportions of phenol.

As already stated under creosote, on page 553, the purer varieties of crude carbolic acid are also known as coal tar creosote, and often sold as commercial creosote. Carbolic acid and wood tar creosote differ, however, so widely in their physical and chemical properties that they can be readily distinguished from each other by the tests given in the Pharmacopœia.

Chemically, carbolic acid belongs to the class of compounds known as phenols, and, being the simplest form thereof, is often designated merely as phenol. The name carbolic acid was given to the substance by Runge, who first isolated it from coal tar, on account of its source (carbo, coal) and its acid properties. Phenols are hydroxyl derivatives of benzene and other hydrocarbons of the aromatic series, and occur as monatomic, diatomic, and triatomic compounds, containing respectively 1, 2, and 3 hydroxyl groups; examples of each class occur in the Pharmacopœia; thus, carbolic acid, C_6H_5OH, resorcin, $C_6H_4(OH)_2$, pyrogallol, $C_6H_3(OH)_3$.

The Pharmacopœia directs that the amount of absolute phenol present in carbolic acid shall be determined volumetrically by precipitation of the phenol as tribromophenol, $C_6H_2Br_3OH$. The solution used for this purpose is known as Koppeschaar's Solution, and is designated in the Pharmacopœia as decinormal bromine solution, although it contains no free bromine; it is a solution of sodium bromate and bromide in such proportions that when treated with hydrochloric acid an amount of bromine is liberated corresponding to 0.007976 Gm. for each cubic centimeter of the solution used, thus constituting it a decinormal bromine solution. In the official test an excess of this solution is added to an aqueous solution of carbolic acid together with some hydrochloric acid, and the excess ascertained by addition of potassium iodide and subsequent titration of the liberated iodine by means of sodium thiosulphate solution. Since iodine is liberated by bromine in exact molecular proportions, a cubic

centimeter of decinormal sodium thiosulphate solution corresponds in value to one cubic centimeter of decinormal bromine solution, and the number of Cc. $\frac{N}{10}$ $Na_2S_2O_3$ solution required to decolorize the iodine solution subtracted from the whole number of Cc. of $\frac{N}{10}$ Br. solution added originally, leaves the number of cubic centimeters of the latter solution necessary for the precipitation of all phenol present as tribromophenol.

Four distinct reactions occur during the performance of this test before the data necessary for the calculation of the percentage of phenol present are obtained, namely: 1. The liberation of bromine by means of hydrochloric acid, thus $NaBrO_3 + 5NaBr + 6HCl = 6NaCl + Br_6 + 3H_2O$; 2. The precipitation of tribromophenol, thus $C_6H_5OH + Br_6 = C_6H_2Br_3OH + 3HBr$; 3. The liberation of iodine, thus $2KI + Br_2 = 2KBr + I_2$; 4. The decoloration of the iodine solution, thus $2Na_2S_2O_3 + I_2 = 2NaI + Na_2S_4O_6$. The second equation shows that 93.78 parts of absolute phenol require 478.56 parts of bromine for complete precipitation; hence each Cc. of the bromine solution corresponds to 0.001563 Gm. of C_6H_5OH, for 478.56 : 93.78 :: 0.007976 : 0.001563. If 0.039 Gm. of carbolic acid be used for the volumetric test, 24 Cc. of decinormal bromine solution will be required to show 96 per cent. of absolute phenol, for 96 per cent. of 0.039 is 0.03744 and $0.001563 \times 24 = 0.037512$.

Among the derivatives of carbolic acid is one, which, although not officially recognized, is extensively employed in medicine, and appears in both the German and British Pharmacopœias, namely, phenacetin. The process for its preparation is a complicated one, paranitrophenol being first obtained by acting on carbolic acid with diluted nitric acid; this is converted into a sodium compound, then into paranitrophenetol by the action of ethyl iodide, and finally into paraphenetidin by means of nascent hydrogen. By boiling with glacial acetic acid paraphenetidin is converted into para-acetphenetidin or phenacetin, $C_6H_4OC_2H_5NHC_2H_3O$. It occurs as a crystalline powder or in the form of colorless scaly crystals, and is sparingly soluble in water.

NAPHTALENE (also written Naphtalin). $C_{10}H_8$. This hydrocarbon exists like benzene in coal tar; it is found in the so-called heavy oil, and is deposited as a dark-colored crystalline substance from the fraction collected between 180° and 250° C. (356° and 482° F.). Crude naphtalene is purified by successive treatment with caustic soda and sulphuric acid, to remove acid and basic by-products, after which it is repeatedly heated with concentrated sulphuric acid, being each time distilled with steam, and is finally resublimed. The white naphtalene thus obtained still has a tendency to darken when exposed to air and light, to overcome which it is treated for a short time with a mixture of sulphuric acid and manganese dioxide at water-bath temperature; finally, the product is washed with weak alkaline solution and water and again sublimed.

For pharmaceutical purposes, naphtalene recrystallized from alcohol should alone be used.

NAPHTOL. $C_{10}H_7OH$. This compound, belonging to the class of phenols, bears the same relation to naphtalene as carbolic acid bears to benzene. Naphtalene, when heated with concentrated sulphuric acid, forms naphtalene sulphonic acid, $HSO_3C_{10}H_7$, of which two varieties occur, designated as alpha and beta naphtalenesulphonic acid; the formation of these two acids depends upon the temperature employed, the alpha acid being produced at water-bath temperature and even below, and changed to the beta variety as the temperature is raised beyond this point. Both acids, when treated with milk of lime, yield the respective calcium naphtalenesulphonates, from which the corresponding sodium salts are obtained by decomposition with sodium carbonate. The sodium salts fused with caustic soda yield sodium naphtol and sodium sulphite, which, by treatment with hydrochloric acid, are converted into sodium chloride and alpha- or beta-naphtol, as the case may be. The final product is further purified by sublimation and recrystallization from water.

The Pharmacopœia recognizes only betanaphtol, and, as alpha-naphtol is far more poisonous than the official variety, the formation of beta-naphtalenesulphonic acid only is sought to be insured by heating the mixture of naphtalene and sulphuric acid to 200° C. (392° F.).

Commercial naphtol is frequently contaminated with the alpha variety, for the detection of which the Pharmacopœia gives a special test, depending upon the production of a crimson color changing to blue, when a 2 per cent. aqueous solution of naphtol is mixed with a trace of sugar and carefully underlaid with concentrated sulphuric acid.

Naphtol furnishes a number of derivative products which have been introduced into medicine, such as benzonaphtol or naphtol benzoate—betol or naphtol salicylate, known also as naphtalol, naphtosalol or salinaphtol—hydronaphtol—asaprol or calcium naphtolsulphonate—alumnol or aluminum naphtolsulphonate, etc. An account of these products and their properties can be found in the National Dispensatory, 5th edition, pp. 1073, 1074.

CHAPTER LIV.

STARCHES, GUMS, AND SUGARS.

BESIDES cellulose, certain other principles are widely diffused in the vegetable kingdom, which are of more or less interest to pharmacists, either as useful medicinal agents or because they must be excluded in the preparation of certain galenicals. These are known as amylaceous, mucilaginous, and saccharine principles, and are usually designated as starches, gums, and sugars. The investigations of Fischer and others regarding the chemical character of these well-known plant-products have so completely changed the view-formerly entertained, and so enriched the knowledge regarding their intimate relationship, that chemists now consider starch, gum, and sugar, and also cellulose, as members of a group designated as saccharides; in regard to their chemical character, they are looked upon as aldehydes, ketones, and anhydrides of certain hexatomic alcohols.

STARCH. This substance occurs chiefly in the seeds, roots, and rhizomes of plants, where it appears deposited for the purpose of future nourishment either of the germinating embryo or during the next year's growth of the plant itself. When viewed with the naked eye, starch appears as a structureless substance in the form of a powder, but under the microscope it is seen to consist of round, ovate, lenticular, or polyhedral granules or cells, differing in size and shape according to the source whence the starch has been taken, as may be seen in Figs. 281 to 286. Starch granules appear to consist of concentric layers of varying density, arranged around a nucleus or hilum situated in the centre of the granule, or more generally at one end or near the margin. The formation of starchy matter and the manner of its deposit belong more properly to the study of physiological botany.

While a valuable dietetic and article of food, starch possesses little or no medicinal virtue, and, as its presence largely interferes with the stability of pharmaceutical preparations, it is sought to be excluded by the use of appropriate menstrua. Starch is insoluble in cold water, strong or diluted alcohol, and ether, but when treated with boiling water solution takes place and a more or less gelatinous mucilage results upon cooling. This peculiar behavior with water is due to the fact that the starch granules have a very hard outer coating (by some authorities looked upon as a distinct membrane), to which the name farinose or amylin has been given; this is ruptured by the boiling water, after which the white contents of the

granule, known as granulose or amidin, are dissolved. Prolonged trituration of starch with sand causes a similar rupture of the farinose, when a portion of the amidin will also be taken up by cold water. Solutions of zinc chloride, calcium chloride, and similar

FIG. 281.

Wheat Starch.

FIG. 282.

Corn Starch.

FIG. 283.

Rice Starch.

FIG. 284.

Potato Starch.

FIG. 285.

Maranta Starch.

FIG. 286.

Curcuma Starch.

salts dissolve starch in the cold. Complete solution of the granules does not occur even with boiling water, as the farinose remains undissolved, but it can be rendered soluble by the action of sulphuric acid. If alcohol be added to starch mucilage, a white powder, soluble in cold water, is precipitated; this is known as soluble starch.

In composition starch is isomeric with cellulose, but differs from it

in physical and many chemical properties. The most delicate reagent for starch is iodine, which strikes a characteristic blue color with cold solutions of starch, and, in the form of solution, is used to detect starch in vegetable tissues. Conversely starch mucilage is extensively employed in iodimetry as an indicator; the union between starch and iodine is, however, a very feeble one, and not considered to be of a chemical character, as it is easily broken up by heat.

When heated to 190° C. (374° F.) with glycerin, starch forms a transparent jelly, known as plasma, which is occasionally used as a vehicle for ointments.

All air-dried starch, when heated at 100° C. (212° F.) to constant weight, loses about 14 per cent. of water, which is gradually reabsorbed by exposure to the air; if anhydrous starch be mixed with a small quantity of water it absorbs the same with evolution of heat, as certain inorganic salts absorb water of crystallization. When heated for some time to 170°–200° C. (338°–392° F.), starch is gradually converted into dextrin and becomes soluble in cold water, losing at the same time its property of being colored blue by iodine. The same result occurs if starch be heated with diluted nitric or sulphuric acid, the change, however, taking place in less time and at a lower temperature; if the action of the diluted acids be allowed to continue for a longer period, the dextrin is finally converted into dextrose (glucose). Diastase, the active ferment of malt, also effects the hydrolysis of starch into dextrin, and finally into a kind of sugar, differing, however, from dextrose, and known as maltose; for this reason starch paste is used in the valuation of malt extracts.

Dextrin is extensively made for the market from potato starch, either by the dry-heat process above mentioned or by mixing the starch into a paste with water acidulated with nitric acid, pressing the paste into cakes, drying, powdering, and heating for one or two hours at 110° C. (230° F.). Dextrin occurs in two varieties, white and yellow, which are soluble in cold as well as hot water, forming a mucilaginous liquid; it has a sweetish taste, peculiar odor, and is also known as British gum. Iodine colors dextrin pink or reddish, unless unaltered starch is present, when a purplish tint results.

Two substances, allied to starch and isomeric with it in composition, are met with in certain drugs; these are lichenin and inulin, the former occurring in cetraria and the latter in inula, taraxacum, etc. Lichenin, also known as moss-starch, is soluble in boiling water and gelatinizes upon cooling; iodine imparts to it a dirty-blue color. Inulin forms a clear solution with boiling water and does not gelatinize upon cooling; continued boiling with water converts it into levulose or inverted sugar. It is colored yellow by iodine and does not occur in the form of concentric layers, nor does it contain a definite and constant proportion of water like starch.

Starch is obtained for use by washing it out from the material containing it with water, the mixture being transferred to large sieves or straining-bags, which allow the starch to pass through with

the water and retain the cellular fibre. In the case of potatoes, these are first grated, while wheat, corn, etc., are treated in the form of flour. Since cereals contain a nitrogenized principle or ferment, called gluten, intimately mixed with the starch, this is removed either by means of incipient fermentation not affecting the starch, or it may be separated by kneading the flour in muslin bags while a stream of water continually falling on it washes out the starch, leaving the gluten behind. The different varieties of starch can be best distinguished from each other by their shape and size under the microscope, but some show also differences in their behavior with hot water and also hydrochloric acid.

Official starch, recognized in the Pharmacopœia by the general Latin term *amylum*, is corn starch, and is used in preparing the official glycerite of starch. Starch was known to the ancients, who applied the name amylum (derived from the Greek word μύλος, a millstone, and the prefix ἀ, meaning privative or without) to the substance, because starch could be obtained without grinding between stones, as in the case of flour.

GUMS. These are amorphous translucent substances, in all probability excretory products, obtained usually as exudations. They differ from starch in being wholly or partly soluble in cold water and in not being colored blue by iodine; the blue coloration produced in tragacanth is due solely to the presence of starch. Gums may be divided into two classes, which differ from each other in physical as well as chemical properties; for convenience they are known as gums and mucilages, respectively. As already stated on pages 185 and 296, gums are precipitated from their aqueous solution by strong alcohol and solutions of ferric chloride and sodium borate and silicate, the precipitate in the last three cases being of a gelatinous character. Diluted alcohol, containing less than 60 per cent. by volume of absolute alcohol, is capable of dissolving gums (the quantity taken up increasing with the decreasing proportion of alcohol present), but glycerin has no solvent effect whatever, although it mixes clear with aqueous solutions of gums. The most delicate reagent for true gum is solution of lead subacetate, which still causes slight opalescence in solutions containing 1 part of acacia in 10,000 parts of water.

True gums consist largely of arabin or arabic acid combined chiefly with calcium, together with potassium and magnesium. Mucilages consist partly of soluble and partly of insoluble principles, and in some cases contain also starch. Acacia and tragacanth are the official representatives of the two classes in the Pharmacopœia, but the mucilages are also met with in althæa, elm bark, linseed, sassafras pith, etc. The soluble portion of tragacanth is not precipitated by alcohol or solution of lead subacetate, like arabin, and the insoluble portion is tinged blue by iodine, as already stated above. The so-called gum exuding from the cherry, peach, and plum trees must also be classed with the mucilages.

Arabin, to which the empirical formula $C_{12}H_{22}O_{11}$ has been assigned, may be obtained from mucilage of acacia, after acidulation with hydrochloric acid, by precipitation with alcohol as a milk-white mass, of acid reaction and liberating carbon dioxide from carbonates. When dried it absorbs water and swells, but does not dissolve until lime-water has been added.

Metarabic acid or cerasin occurs in the insoluble portion of cherry gum, and may be obtained from acacia by heating the same for some time at 100° C. (212° F.); it is soluble in alkaline liquids.

Parabin, which is isomeric with arabin, is found in agar-agar or Ceylon moss; it is without acid reaction, swells up to a jelly with water, and is dissolved by dilute mineral acids, but precipitated by alkalies and alcohol.

Bassorin is the name given to the pectin-like principle present in tragacanth and allied products. It is insoluble in cold and hot water, but absorbs the same, swelling to a gelatinoid mass, and is soluble in alkaline liquids. Besides bassorin, the mucilages also contain soluble principles, and in some cases unaltered starch; the former are not identical with arabin, being without acid reaction.

If tragacanth be moistened with a solution of pyrogallol it gradually blackens, whereas acacia similarly treated develops a red color, due to the formation of pyrogalloquinone.

Carragheen is the mucilaginous constituent of Irish moss, or chondrus. It is not precipitated by alcohol, and by treatment with diluted sulphuric acid yields galactose.

When treated with boiling nitric acid, gums are converted into mucic, saccharic, and oxalic acids. By continuous boiling with water acidulated with sulphuric acid, some gums yield arabinose and others galactose, products closely allied to the sugars; of these, galactose is capable of fermentation, while arabinose is unfermentable.

The name gum is derived from the Greek word *κομμι*, and this from the Egyptian name kami, applied to acacia, which was used nearly 4000 years ago as an adhesive agent in painting.

Very closely allied to the gums are the pectous substances. Unripe acidulous fruits and certain succulent roots contain a peculiar body called pectose, which, under the influence of a ferment known as pectase in connection with light and heat, and, in the case of fruits, of organic acids also, is changed into pectin, and finally into pectosic acid or vegetable jelly, to which is due the gelatinization of certain fruit juices as well as the infusions of gentian, taraxacum, senega, and other roots. The alkali salts of pectosic acid being soluble, advantage is frequently taken of this in pharmaceutical preparations to prevent gelatinization; as, for instance, the use of ammonia water in fluid extract of senega.

Unripe green fruits owe their hardness to the presence of pectose, and become softer as the latter is gradually changed to pectin during the ripening process.

The name pectin is derived from the Greek word πηκτός, meaning curdled.

SUGARS. Although for pharmaceutical purposes but three kinds of sugar are employed, chemists include under the general term of sugars a much larger class of compounds, belonging to the carbohydrates and characterized by a more or less sweet taste. For convenience, sugars are divided into two main groups, known as glucoses and saccharoses.

GLUCOSES are looked upon by chemists as aldehydes and ketones, derived from the alcohols mannitol and dulcitol, $C_6H_8(OH)_6$; they contain two atoms of hydrogen less than these compounds, and, in some cases at least, are convertible into hexatomic alcohols by the action of nascent hydrogen. They can be obtained by hydrolysis from various other carbohydrates, and with few exceptions are directly fermentable. As a rule, they crystallize imperfectly or with difficulty. The empirical formula, $C_6H_{12}O_6$, has been assigned to the members of this group, which includes dextrose, levulose, galactose, arabinose, sorbinose, etc.

Dextrose is the best known member of the glucose group, occurring in commerce both in the fluid and solid form; to the former the term glucose is usually applied, while the solid variety is better known as grape-sugar. In nature dextrose is found associated with levulose or fruit-sugar in numerous fruits and in honey; it also occurs in certain secretions of the human body as the result of a disease known as diabetes mellitus. Artificially, it is manufactured on a large scale from corn starch by treatment with diluted sulphuric acid, the process being conducted in both open and closed converters, of which the latter require the application of a higher heat but a shorter time to complete the change. As already stated on page 563, the first action of the diluted acid is to change the starch into dextrin, which is finally converted into dextrose; liquid or syrupy glucose usually contains both dextrin and dextrose, while in the solid grape-sugar the complete conversion into dextrose has been carried out. Corn starch is always mixed with gluten, which is removed by treatment with caustic soda, after which the starch is mixed with water to a creamy consistence and run into the diluted acid and heated by means of steam until all starch has been converted; the acid is then neutralized by means of calcium carbonate and the liquid filtered, passed through animal charcoal, and concentrated.

Grape-sugar separates as a granular crystalline deposit in honey, and can be obtained in a hydrated form in small, wart-like crystals from its aqueous or hydro-alcoholic solution; from a hot solution in alcohol or methylalcohol it separates in anhydrous prismatic crystals. It is soluble in very nearly its own weight of water and in fifty parts of alcohol at 15° C. (59° F.), the solutions possessing a far less sweet taste than those of ordinary sugar. At 60° C.

(140° F.) grape-sugar softens, and at 86° C. (186.8° F.) melts completely.

On account of its remarkable reducing properties, dextrose has been used with success in the preservation of certain ferrous solutions, notably the syrup of ferrous iodide. It readily reduces ferric and cupric compounds to the ferrous and cuprous state, and the salts of bismuth and silver to the metallic condition.

Various tests can be used for the detection of dextrose, such as Trommer's test (cupric sulphate, solution of potassa, and heat), causing a deposit of brick-red cuprous oxide; Moore's test (solution of potassa and heat), causing a dark, almost black color; Boettger's test (bismuth subnitrate, solution of potassa, and heat), causing a black precipitate of metallic bismuth, and others. For the quantitative determination of dextrose, volumetric alkaline solution of cupric tartrate, known as Fehling's Solution, is usually employed; each cubic centimeter of this solution corresponds to 0.005 Gm. of anhydrous dextrose. When Fehling's Solution is boiled in the presence of dextrose, yellowish hydrated cuprous oxide is first formed, which is finally changed into the anhydrous brick-red variety. Since dextrin also reduces the cupric salt of Fehling's Solution, its absence must first be determined in quantitative determinations. Barfoed's Solution, consisting of 13.3 Gm. of crystallized cupric acetate and 2 Gm. of glacial acetic acid in 200 Cc. of water, suffers reduction with all glucoses, but not with dextrin.

The name dextrose was given to this particular sugar on account of its dextro-rotatory power, since it invariably deflects the ray of polarized light to the right when examined by means of a polariscope. An explanation of the uses of the polariscope can be found on pages 512 and 513 of the Pharmacopœia.

Levulose, or fructose, is of interest chiefly as a natural constituent of honey; it also occurs associated with dextrose in many fruits, and is therefore known as fruit-sugar. The name levulose was given it because it is lævo-rotatory—that is, causes the plane of polarized light to deviate to the left. When pure, it occurs as a colorless or faintly yellowish syrup of very sweet taste which crystallizes with great difficulty; it remains in the liquid portion of honey after all the grape-sugar has been removed. As stated under Starch, levulose is also formed by prolonged boiling of inulin with diluted acids. The term inverted sugar is usually applied to the mixture of dextrose and levulose, whether obtained by inversion of cane-sugar by means of diluted acids and heat, or by some special ferment, such as that supplied by the bees in the manufacture of honey.

Natural honey contains from 65 to 80 per cent. of a mixture of dextrose and levulose, together with small portions of cane-sugar, besides 20 or 30 per cent. of water and about $\frac{1}{10}$ per cent. of formic acid. During the clarification of honey the acid is generally dissipated, and possibly on this account clarified honey is more prone to fermentation than the crude article. Commercial honey is frequently

adulterated with a solution of glucose and dextrin; the latter can be detected by addition of an excess of official alcohol to an aqueous solution of honey. Any dextrin present will be precipitated in the form of white flocculi.

SACCHAROSES appear to be the result of a union of two molecules of one or any two members of the group of glucoses, water being eliminated at the same time, hence they may be considered as anhydrides; thus, $2C_6H_{12}O_6 = C_{12}H_{22}O_{11} + H_2O$. In support of this view, the members of this group have been found to take up water and split up into equal molecules of glucoses if heated with diluted acids. Saccharoses are darkened by strong sulphuric acid, and form colorless combinations with the alkalies, differing in these respects from the glucoses. The more important members of the group are sucrose or cane-sugar, lactose or milk-sugar, and maltose or malt-sugar; mycose, identical with trehalose, is of some interest as occurring in ergot. With the exception of malt-sugar, the saccharoses can only be fermented after previous conversion into one of the glucoses.

Sucrose, or cane-sugar, officially recognized as Saccharum, is obtained from sugar-cane, sorghum, and the common European sugar-beet. While immense quantities of sugar are prepared in this country direct from the juice of the cane, considerable amounts are also imported in the form of raw or crude sugar for refining purposes.

The juice of the sugar-cane contains about 18 per cent. of sugar and 81 per cent. of water, besides traces of salts, mucus, albumen, etc. Having been expressed, it is mixed with milk of lime and heated, the greenish scum rising to the surface being removed; the liquid is then strained, concentrated, and stirred while crystallizing, so as to prevent the formation of large crystals. The crystalline mass is placed into perforated hogsheads to allow the mother-liquor, molasses, to drain off, after which it is redissolved, the solution decolorized by filtration through animal charcoal, concentrated by evaporation in vacuum-pans at about 80° C. (176° F.), and crystallized. Finally, the crystals are drained and dried by means of large centrifugals, wherein the adhering mother-liquor, containing also inverted or so-called non-crystallizable sugar, is rapidly removed.

The sugar-beet contains about 8 or 10 per cent. of sugar, which is obtained by a process similar to the above, the juice being treated with lime, filtered through charcoal, concentrated, and crystallized.

Sucrose is soluble in half its weight of water at 15° C. (59° F.), and in 175 parts of alcohol at the same temperature; it is thus seen to be more soluble in water and less soluble in alcohol than glucose. A saturated solution of cane-sugar at 15° C. (59° F.) contains 67.72 per cent. of sugar and has a specific gravity of 1.345; one liter contains 910.8 Gm. of sugar and 434.2 Gm. of water. Official syrup is, therefore, a little less than saturated, containing 64.54 per cent. of sugar. While dextrose melts at 80° C. (176° F.), dry cane-sugar remains unaltered at this temperature, but melts at 160° C. (310° F.),

congealing afterward to a slightly colored, glassy mass. Heated to 180° C. (356° F.), cane-sugar splits up into dextrose and a product isomeric with starch and dextrin, known as levulosan; above 205° C. (401° F.), a dark-brown, thick liquid of complex composition and bitter taste results, to which the name caramel has been given.

If cane-sugar be heated with diluted (5 per cent.) sulphuric acid it is changed into inverted sugar, a mixture of equal molecules of dextrose and levulose, and is only then capable of fermentation; certain ferments produce the same effect. Sucrose is always dextro-rotatory, but becomes less so after inversion, as the levulose then present exercises its lævo-rotatory effect on the plane of light.

The purest sugar obtainable is that known as cut loaf sugar, which is the best kind for the preparation of syrups and similar solutions, but is not so convenient for use as granulated sugar; the latter, however, is generally contaminated with ultramarine, the blue color of which is intended to overcome the natural yellowish tint of the sugar.

The official test for the presence of grape-sugar in cane-sugar depends upon the reduction of the silver nitrate to the metallic state by the dextrose, as pure cane-sugar is without effect upon it.

Cane-sugar is used as a valuable preservative for many otherwise unstable solutions, and its sweet taste renders it a desirable adjuvant in prescriptions. It is also known to increase the solubility of several metallic oxides and vegetable principles.

Lactose, or sugar of milk, which is recognized in the Pharmacopœia by the latter name (Latin name, saccharum lactis), is obtained from the milk of mammalia, where it is found to the extent of from 3 to 6 per cent. It is said also to exist in the fruit of Achras sapota, a tree of the West Indies, this being the only known case of its occurrence in the vegetable kingdom. Milk-sugar is obtained by crystallization from the whey or thin fluid remaining after removal of the casein or albuminous principle by coagulation. The crude granular product is purified by resolution, filtration, and recrystallization. Formerly the world's supply was furnished by Europe, chiefly Switzerland, but now considerable quantities are manufactured in this country.

The crystals of sugar of milk contain 5 per cent. of water, which is not lost until a temperature of 130° C. (266° F.) is reached. They are very hard, and require about 6 or 7 parts of water for solution, the solution being far less dense than one of dextrose or cane-sugar of equal concentration, and far less sweet in taste. As found in the shops, sugar of milk is always in the form of powder, which feels gritty between the teeth. In pharmacy, it is used exclusively as a diluent in the preparation of triturations, powdered extracts, etc., for which purposes it is admirably adapted, as it is non-hygroscopic.

Like dextrose, sugar of milk is dextro-rotatory, and also reduces an alkaline solution of cupric tartrate, but does not reduce Barfoed's Solution of cupric acetate (see page 567). Boiled with diluted acids,

sugar of milk yields dextrose and galactose; the latter crystallizes in large prisms and yields mucic acid, insoluble in cold water when treated with nitric acid, whereas dextrose yields saccharic acid, which is soluble.

Maltose, or malt sugar, is produced by the action of diastase of malt on starch, either during the germination of the barley, or when diastase is mixed with starch and water and kept at a temperature of 70° C. (158° F.). It is directly fermentable, and is of considerable interest in pharmacy on account of the part it plays in the fermentation of grain in the manufacture of alcohol. Maltose crystallizes with one molecule of water, and is readily soluble in water; although strongly dextro-rotatory, it can be distinguished from dextrose, like milk-sugar, by means of Barfoed's Solution.

CHAPTER LV.

ALCOHOL AND ITS DERIVATIVES.

ALTHOUGH, in chemistry, the term alcohol is used to designate a group of compounds derived from hydrocarbons of the methane or fatty series, by replacement of one or more hydrogen atoms by a corresponding number of hydroxyl groups, which have certain chemical properties in common, it is restricted in pharmacy to one substance, chemically known as ethyl alcohol, and recognized in the Pharmacopœia also by the simple term alcohol. When other alcohols are used in pharmacy they are either designated by specific names, such as glycerin, mannitol, etc., or by adding a qualifying prefix to the word alcohol, as amyl alcohol, methyl or wood alcohol, etc., to distinguish them from ordinary or ethyl alcohol.

Alcohol is obtained in this country almost exclusively from grain, while in Europe potatoes are extensively employed, by a process known as vinous fermentation. Fermentation is a process of decomposition differing from putrefaction in that the resulting products are, as a rule, valuable, or at least useful and not accompanied by offensive gases; fermentation is usually applied to the decomposition of substances composed of carbon, hydrogen, and oxygen; while, if nitrogen and sulphur are also present, the term putrefaction is more aptly used, on account of the putrid or foul odor emitted by such bodies during decomposition. Certain conditions are essential to both processes of decomposition, namely, the presence of air, moisture, heat, and certain agents known as ferments. There are fermentations of various kinds, such as saccharine, vinous, mucic, lactic, butyric, and acetous, depending upon the substances under manipulation, some of these being in reality oxidation processes not due to fermentative action.

In the manufacture of alcohol, the first step necessary is the saccharine fermentation, known also as the mashing process, which consists in the conversion of starch into sugar by means of diastase. This latter substance is produced during the germination of grain, as in the malting of barley. Malt is made by well moistening barley with water and spreading it, about two feet deep, on stone floors, in dark rooms; heat is developed, and partial germination is allowed to go on, during which time diastase is produced, the barley assuming a darker color and peculiar odor, while the starch of the grain is converted into dextrin and maltose or malt sugar. Diastase is capable of converting 2000 times its weight of starch into maltose. When isolated, it is a white, tasteless, solid, soluble in water and weak

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alcohol, but precipitated by strong alcohol, and rendered inert by the heat of boiling water.

Extract of malt, which, if properly made, should represent good malt in the form of a concentrated infusion, owes its value as a digestive agent solely to the diastase present; therefore that extract capable of converting the largest amount of starch into dextrose is unquestionably the best. The following method is recommended for comparative testing of malt extracts: Dissolve 5 Gm. of extract of malt in sufficient distilled water to yield 100 Cc. of solution; of this, add 5 Cc., representing 0.25 Gm. of the extract, to 250 Cc. of cold starch mucilage (prepared by dissolving 30 Gm. of Bermuda Arrow Root in 1000 Cc. of boiling distilled water) and keep the mixture at a temperature of 55°–60° C. (131°–140° F.) for 30 minutes; then stop the diastatic action, by raising the temperature to 100° C. (212° F.) or by addition of 2 or 3 Cc. of a 10 per cent. sodium hydroxide solution, and dilute the mixture to a given volume by addition of water. Titrate an aliquot part of the liquid with Fehling's Solution (alkaline cupric tartrate volumetric solution, U. S. Ph.) and ascertain the amount of dextrose present, from which deduct the amount found in a corresponding amount of the extract of malt by previous titration with Fehling's Solution; the difference indicates the amount of sugar produced by the diastase present in the extract. Each Cc. of Fehling's Solution corresponds to 0.005 Gm. of anhydrous dextrose, or 0.0045 Gm. of starch converted thereinto.

During the mashing process large quantities of raw grain are kept in contact with malt and water at a moderately elevated temperature, whereby the starch is gradually all converted into dextrose, apparently by the simple appropriation of water, as shown by the following equations:

$$1.\quad \underset{\text{Starch}}{3C_6H_{10}O_5} + H_2O = \underset{\text{Maltose}}{C_{12}H_{22}O_{11}} + \underset{\text{Dextrin}}{C_6H_{10}O_5}$$

$$2.\quad \underset{\text{Maltose}}{C_{12}H_{22}O_{11}} + \underset{\text{Dextrin}}{C_6H_{10}O_5} + 2H_2O = \underset{\text{Dextrose}}{3C_6H_{12}O_6}$$

The saccharine solution thus obtained is known as wort, and, after addition of some yeast, is allowed to undergo fermentation at a temperature which is maintained between 15° and 30° C. (59° and 86° F.), whereby a weak alcoholic liquid is produced, due to the splitting up of dextrose into alcohol and carbon dioxide, thus: $C_6H_{12}O_6 = 2C_2H_5OH + 2CO_2$. Besides alcohol and carbon dioxide, however, some amyl alcohol and other homologous products, collectively designated as fusel oil, are also produced, and Pasteur has shown that small quantities of glycerin (3 per cent.) and succinic acid (0.6 per cent.) are invariably formed. The composition of these so-called low wines or weak spirits varies with the starchy material used in their manufacture; thus, potato starch always yields a much larger proportion of amyl alcohol than grain starch, while grain spirit is contaminated with œnanthic and other ethers.

Distillation of the fermented liquid furnishes a product much richer in alcohol, raw whiskey, which is then further rectified by treatment with recently burned charcoal and subsequent redistillation in stills provided with a series of condensers, in the first of which much of the water and amyl alcohol is retained, allowing a purer and stronger alcohol to pass on to the other condensers. For the further removal of water and foreign odors from alcohol, distillation over sodium manganate, anhydrous sodium acetate and freshly burned lime is employed.

During the past two or three years alcohol has been successfully produced from cellulose by treating dried peat with very dilute sulphuric acid for several hours at a temperature of 120° C. (248° F.), whereby peat-sugar is formed, which is subsequently fermented with yeast and distilled, yielding as much as 62 liters of absolute alcohol for 1000 kilogrammes of dry peat used (about 15 gallons for each ton).

The Pharmacopœia recognizes four different grades of strength of alcohol, designated by specific names, thus:

PERCENTAGE OF TRUE ETHYL ALCOHOL.

		Percentage by weight.	Percentage by volume.
Alcohol	about	91.0	94.0
Absolute alcohol		99.0	99.5
Deodorized alcohol . . .	about	92.5	95.1
Diluted alcohol . . .	about	41.0	48.6

Whenever alcohol and water are mixed, heat is evolved and contraction of volume results, both varying with the proportions of the two liquids used. According to Flückiger, the rise of temperature will be greatest when 30 parts by weight of absolute alcohol are mixed with 70 parts by weight of water, amounting to 9° C, or 16.2° F., and the greatest contraction occurs when 58 volumes of absolute alcohol are mixed with 54 volumes of water, amounting to a loss of 4 volumes or 3.57 per cent. of the total mixture.

The use of the alcoholometer for ascertaining the percentage strength of commercial alcohol has already been fully explained on page 57 and rules have been given on pages 93 and 94 for preparing weaker alcohol from a stronger variety by dilution with water. Besides the Pharmacopœia gives specific directions, under Diluted Alcohol, for preparing mixtures of definite strength.

Commercial alcohol does not always come up to the requirements of the Pharmacopœia for official alcohol, averaging, as a rule, from 91 to 92 per cent. by volume of ethyl hydroxide; but the variety sold as Cologne spirit generally contains 94.5 or 95 per cent.; the latter also corresponds more closely to the official deodorized alcohol in its freedom from foreign odor. Alcohol which has been stored for some time in barrels, particularly if the latter have been imperfectly charred on the inside, is apt to be contaminated with coloring matter and tannin.

Absolute alcohol is intended to be identical with deodorized alcohol as far as the absence of amyl alcohol and other impurities is concerned, but contains far less water than the latter, the Pharmacopœia not allowing more than 1 per cent. by weight. The entire absence of traces of moisture is practically impossible, although the amount is reduced to less than ½ per cent. by some manufacturers. Among the various dehydrating agents suggested, freshly burned lime has been found most desirable. Deodorized alcohol is either shaken with the lime in coarse powder, for some time, or caused to percolate repeatedly through alternate layers of fine and coarse granules of lime, in an apparatus so arranged as to avoid all contact with air, after which it is transferred, without exposure, to a column still and distilled at a low temperature, under reduced pressure, by which means it is possible to carry the alcohol vapor forward through several condensing chambers, in which any aqueous moisture still remaining will be separated and flow back into the still. Absolute alcohol is very hygroscopic and should be preserved in tightly stoppered bottles containing either some anydrous cupric sulphate or pieces of freshly burned lime. In pharmacy its use is confined to that of a solvent for phosphorus and similar substances, but in the manufacture of certain chemicals it is more extensively employed.

Official diluted alcohol, a most valuable solvent for many vegetable principles, is made by mixing equal volumes of official alcohol and water. Since the mixture suffers nearly 3 per cent. loss by contraction, the finished, cooled product contains about 48.4 per cent. by volume of absolute ethyl alcohol. It should not be used until the temperature of the mixed liquids has again fallen to that of the room.

Proof spirit, as recognized by the U. S. government, contains 50 per cent. by volume of absolute alcohol, and is reckoned by gaugers as equivalent to 100 degrees; hence the terms 25 or 40 above or below proof do not refer to alcoholic liquids containing 25 or 40 per cent. of alcohol more or less than the 50 per cent. proof spirit, but only one-half as much, namely, 12.5 or 20 per cent. each proof degree, representing ½ per cent. of absolute ethyl alcohol. Official 94 per cent. alcohol is thus said to stand at 188 degrees, or 88 degrees above proof.

Amyl Alcohol, although not recognized in the Pharmacopœia, is of interest as the source of amyl nitrite and valerianic acid and as a valuable solvent used in chemical research. As already stated on page 572, amyl alcohol and other homologous products are formed during the fermentation of grain or potato starch; larger quantities may be obtained by continuing the distillation after ethyl alcohol ceases to come over. Amyl alcohol is purified by fractional distillation and repeated washing with a concentrated solution of table salt. It is a colorless, thin, oily liquid of about the same specific gravity as alcohol, but boiling, when pure, at 132° C. (269.6 F.). Chemically

it is amyl hydroxide, $C_5H_{11}OH$, and yields compounds homologous with those of ethyl alcohol—namely, amyl ether, $(C_5H_{11})_2O$, amyl aldehyde, $C_5H_{10}O$, and valerianic acid, $C_5H_{10}O_2$.

DERIVATIVES OF ALCOHOL. The following preparations made from ethyl alcohol are officially recognized in the Pharmacopœia, and therefore of special interest to pharmacists: Ether, acetic ether, ethereal oil, spirit of nitrous ether, paraldehyde, chloroform, chloral hydrate, and iodoform. In addition, a few allied and some unofficial preparations will also be considered.

ETHER. The general term ether is used by chemists to designate anhydrides of alcohols, or oxides of hydro-carbon radicals; both simple and mixed ethers are known, as the oxygen may be united to two groups of the same or mixed radicals; thus, $(C_2H_5)_2O$, ethyl ether, and $(CH_3)_2O$, methyl ether, are simple ethers, while $(CH_3C_2H_5)O$, methyl ethyl ether, is a mixed ether.

The Pharmacopœia recognizes but one compound by the name ether (Latin name, *æther*), namely ethyl ether or ethyl oxide $(C_2H_5)_2O$, and in all official formulas and physicians' prescriptions this substance is to be understood as intended. Ethyl ether is sometimes called sulphuric ether, and several commercial varieties, known as concentrated and washed ether, are found on the market; but, as their strength and purity are not stated on the label, they should not be used in place of the official ether. The process of ether manufacture consists in heating a mixture of alcohol and sulphuric acid in a suitable still, by means of steam coils, to 130° C. (266° F.) and, when the distillation of ether begins, allowing a continuous supply of alcohol to flow into the still from a feed-back so regulated that the mixture shall be kept at a constant quantity and temperature. The vapors are passed through two purifiers, the first one of cast iron containing a solution of potassa, in which water and other impurities are washed out; the second one of block tin is provided with a bed of pebblestones, where alcoholic and other vapors having a higher boiling point than ether are recondensed and carried to the feed-back near the still. In order that no ether may be lost, both purifiers are kept heated, the purified ether vapor being finally condensed in a large worm surrounded by running water.

Etherification may be thus explained: when alcohol and sulphuric acid are mixed together, one molecule of each combines to form ethylsulphuric acid and water, $C_2H_5OH + H_2SO_4 = C_2H_5HSO_4 + H_2O$. In the presence of heat and an excess of alcohol a further reaction ensues, ether being produced and sulphuric acid regenerated, thus, $C_2H_5HSO_4 + C_2H_5OH = (C_2H_5)_2O + H_2SO_4$.

The theoretical yield of ether amounts to nearly five pounds for each gallon of alcohol used, but in practice rarely more than four pounds are recovered. It is important that the temperature be kept between 130° and 138° C. (266° and 280.4° F.), so as to avoid the

distillation of much alcohol vapor and the formation of other compounds. Since sulphuric acid is continually regenerated its power of etherifying alcohol is theoretically without limit, but in practice it is found that water and other impurities in the alcohol gradually interfere, the acid being diluted and becoming black while the mixture in the still begins to froth. According to Dr. Squibb, a charge of 360 pounds of concentrated sulphuric acid is sufficient for the etherification of 120 barrels of good, clean alcohol.

Official ether has a specific gravity of 0.725 to 0.728 at 15° C. (59° F.) and contains 96 per cent. of absolute ethyl oxide; the remaining 4 per cent. consist of alcohol and traces of water which it is impracticable to remove. It is best preserved in tin containers holding from 100 Gm. upward, as they are less liable to breakage than glass. Ether is very inflammable, and its vapor, which is about two and a half times as heavy as air, when mixed with the latter explodes in contact with flame, hence care is necessary in handling and dispensing ether, especially at night.

Besides being used in various official manufacturing processes, ether also enters into the composition of two alcoholic solutions, designated in the Pharmacopœia as spirit of ether and compound spirit of ether (see page 238), which should be prepared by the pharmacist himself, on account of the variable quality of the commercial articles.

Acetic Ether. This compound is not an ether in a chemical sense, but an ester, or ethereal salt, the basylous hydrogen in acetic acid having been replaced by the ethyl group. Much of the acetic ether found on the market is of inferior quality, and, as its manufacture presents no difficulties, the following process of Hager is recommended, the author having repeatedly used it with much satisfaction: 126 Gm. of official alcohol are mixed with 218 Gm. of 94 per cent. or 222 Gm. of official (92.5 per cent.) sulphuric acid, and the mixture allowed to stand for two or three days in a well-closed flask, so that ethylsulphuric acid may form. Having rendered a quantity of sodium acetate anhydrous, by heating at 130° C. (266° F.) to constant weight, 164 Gm. of this acetate, in powder, are placed in a retort and the acid-alcohol mixture carefully added. The retort is heated in a water-bath and the vapors condensed in a well cooled receiver as long as a brisk reaction continues; the final distillate is collected separately, as it is likely to be more largely contaminated with acetic acid. The reactions occurring in the foregoing process may be illustrated by the equations, $C_2H_5OH+H_2SO_4=C_2H_5HSO_4+H_2O$ and $C_2H_5HSO_4+NaC_2H_3O_2=C_2H_5C_2H_3O_2+NaHSO_4$.

Crude acetic ether is always more or less contaminated with alcohol and acetic acid, which are removed by repeatedly agitating the ether with one-third of its volume of a 20 per cent. sodium chloride solution containing also 2 per cent. of sodium carbonate and carefully decanting the ethereal layer. Milk of lime and caustic alkalies cannot be used, since the acetic ether would thereby be decomposed

and converted into alcohol and the respective acetate. For the removal of water, the purified ether is well shaken for some time with freshly ignited potassium carbonate and redistilled in a water-bath; dehydrated acetic ether is far more stable than that containing water.

Official acetic ether should be neutral to litmus paper, contain not less than 98.5 per cent. of ethyl acetate and be soluble in not less than eight parts of water at 15° C. (59° F.); absolute ethyl acetate requires about 16.5 parts of water for solution.

Ethereal Oil. This name is applied in the Pharmacopœia to a volatile liquid composed of equal volumes of so-called heavy oil of wine and ether. Heavy oil of wine is a complex mixture of ethyl sulphate, $(C_2H_5)_2SO_4$, and varying proportions of certain polymeric hydrocarbons, etherin and etherol; by some, ethyl sulphite, $(C_2H_5)_2SO_3$, is also supposed to be present. The official directions for preparing heavy oil of wine are to distil a mixture of equal volumes of alcohol and sulphuric acid (previously allowed to stand for twenty-four hours, partly to separate lead sulphate), on a sand-bath, at a temperature between 150° and 160° C. (302° and 320° F.), as long as oily drops pass over. The ethereal liquid is separated from the distillate and exposed to the air to free it from ether, after which, it is drained on a well-wetted filter and washed with cold water. Pure heavy oil of wine is a yellowish, somewhat thick, oily liquid of a peculiar aromatic odor and having a specific gravity of 1.13 at 15° C. (59° F.). Diluted with an equal volume of ether, it constitutes official ethereal oil, a pale yellowish liquid, of 0.910 spec. grav. at 15° C. (59° F.).

Ethereal oil is used solely in the preparation of the official compound spirit of ether, in which it is present to the extent of 2.5 per cent. by volume (see page 238).

Much confusion exists regarding the so-called ethereal oil and heavy oil of wine of different manufactures, and some care is necessary in the purchase of the commercial article. As the yield of heavy oil of wine does not average over two per cent. of the weight of alcohol used, it stands to reason that careful producers cannot furnish true ethereal oil at low figures.

Spirit of Nitrous Ether. The official preparation of this name is an alcoholic solution of ethyl nitrite, $C_2H_5NO_2$, yielding, when freshly made, not less than eleven times it own volume of nitric oxide gas.

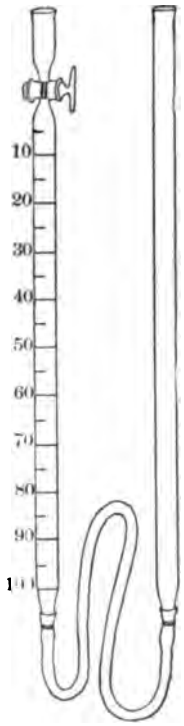
In the pharmacopœial process of manufacture the first step is the preparation of ethyl nitrite by acting on a solution of sodium nitrite with sulphuric acid in the presence of alcohol; the nitrous acid liberated attacks the alcohol, forming ethyl nitrite, which distils over, and water, thus $C_2H_5OH + HNO_2 = C_2H_5NO_2 + H_2O$.

The ethereal distillate is next washed with ice-cold water and afterward with ice-cold sodium carbonate solution, then well shaken with anhydrous potassium carbonate for the purpose of dehydration, and

finally filtered into sufficient deodorized alcohol to make the weight of the finished solution equal to twenty-two times the weight of purified ethyl nitrite obtained. The advantages of this process over those formerly employed consist in the absence of nitric acid and consequent less production of aldehyde and in the better control of action by the use of sodium nitrite in solution and diluted sulphuric acid. The reaction occurring can be illustrated by the following equation: $2NaNO_2 + 2C_2H_5OH + H_2SO_4 = 2C_2H_5NO_2 + Na_2SO_4 + H_2SO_4$.

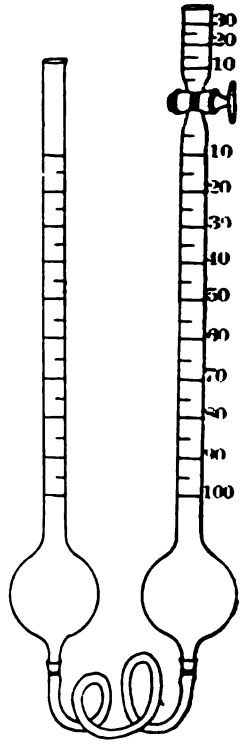
Some years ago a method was suggested by Messrs. Dunstan & Dymond in England, for preparing ethyl nitrite from sodium nitrite, without the aid of heat, by introducing a well-cooled mixture of

FIG. 287.



Lunge's Nitrometer.

FIG. 288.



Curtman's Nitrometer.

sulphuric acid, alcohol, and water, by means of a long thistle tube, to the bottom of a narrow glass vessel containing a strong solution of sodium nitrite and surrounded with ice and salt. The newly-formed ethyl nitrite separates rapidly and floats as a yellowish layer on the saline solution, whence it can be removed by decantation or with a siphon and purified as in the official process. The product

is said to be far less contaminated than when made by distillation, and the process is expeditious and convenient.

By some pharmacists spirit of nitrous ether is made by mixing ethyl nitrite, purchased on the market, with alcohol, but it should be borne in mind that ethyl nitrite readily deteriorates by keeping. If the ethyl nitrite be of good quality and freshly prepared, this is a convenient plan for preparing small quantities of the official solution.

The Pharmacopœia directs the assay of spirit of nitrous ether to be made by gasometric estimation, the nitric oxide obtainable from a given volume of the spirit being evolved and measured over a saturated solution of table salt in a graduated tube or nitrometer (see Figs. 287 and 288); full details of the process are given on pages 509 and 510 of the Pharmacopœia. The equation, $C_2H_5NO_2 + KI + H_2SO_4 = C_2H_5OH + KHSO_4 + I + NO$, shows that 74.87 Gm. of pure ethyl nitrite will yield 29.97 Gm. of nitric oxide measuring at 0° C. (32° F.) 22320 Cc.; hence each Cc. of NO gas at 0° C. (32° F.) must correspond to 0.0033543 + Gm. of $C_2H_5NO_2$, for $74.87 \div 22320 = 0.0033543 +$. As already stated in connection with the valuation of sodium nitrite, on page 450, 1 Cc. NO gas at 15° C. (59° F.) weighs 0.0012727 Gm. and at 25° C. (77° F.), 0.00123 Gm.; therefore, since 29.97 Gm. of nitric oxide gas represent 74.87 Gm. of ethyl nitrite, each Cc. of the gas at 25° C. (77° F.) must correspond to 0.003072 + Gm. of true $C_2H_5NO_2$; for 29.97 : 74.87 :: 0.00123 : 0.003072 +. The quantity of ethyl nitrite corresponding to each Cc. of nitric oxide gas at any other temperature can be readily ascertained by dividing 0.001342656, the weight of 1 Cc. NO gas at 0° C. (32° F.) by the expansion of 1 Cc. of a gas for the given temperature (see page 510 U. S. Ph.), multiplying the quotient so obtained by 74.87 and dividing the product by 29.97.

When strict accuracy is desired in gasometric estimations it becomes necessary also to make a correction of the gas volume for deviation from normal barometric pressure, which is 760 Mm. or 29.87 + inches. As the volume of all gases is inversely proportional to the pressure applied, any volume multiplied by the pressure, expressed in millimeters or inches and then divided by 760 or 29.87, as the case may be, will express the true volume under normal pressure. Thus 50 Cc. of NO gas under 782 Mm. pressure will correspond to 51.44 + Cc. under normal pressure; for 760 : 782 :: 50 : 51.44 +. Such correction of volume for pressure must be applied to the expansion of 1 Cc. for the given temperature before ascertaining the equivalent weight of ethyl nitrite, thus 1.091575 Cc. NO gas at 25° C. (77° F.) under 782 Mm. pressure is equivalent to 1.123173 Cc. at the same temperature under normal pressure; for 1.091575 multiplied by 782 and divided by 760 is equal to 1.123173.

Having acertained the weight of ethyl nitrite corresponding to 1

Cc. of NO gas under the conditions existing at the time of making the assay, the number of Cc. of NO gas obtained from the sample used multiplied by such weight at once expresses the total weight of ethyl nitrite present, which multiplied by 100 and divided by the weight of the sample used (ascertained by multiplying the volume by the specific gravity of the sample) expresses the percentage of true ethyl nitrite found.

Some authorities prefer to reduce the volume of nitric oxide gas obtained at any given temperature and pressure direct to the corresponding volume at 0° C. (32° F.) and 760 Mm. pressure and then multiply the number of cubic centimeters so obtained by 0.0033543, the weight in grammes of ethyl nitrite corresponding to 1 Cc. NO gas under normal conditions, and from this product calculate the percentage of $C_2H_5NO_2$ in the sample, as indicated in the preceding paragraph.

In the official test 5 Cc. of spirit of nitrous ether are used, which should yield not less than 55 Cc. of NO gas at 25° C. (77° F.) to show at least 4 per cent. of pure ethyl nitrite. At 25° C. (77° F.) each Cc. NO, as shown above, corresponds to 0.003072 Gm. C_2H_5-NO_2, hence 55 Cc. represent 0.16896 Gm. If the sample of spirit of nitrous ether be of the average specific gravity stated in the Pharmacopœia, the 5 Cc. used will weigh 4.195 Gm. for $5 \times 0.839 = 4.195$, and to ascertain the percentage of ethyl nitrite found it is necessary to multiply 0.16896 by100 and divide by 4.195, which yields 4 per cent.

Commercial spirit of nitrous ether is often of very inferior quality, since it is frequently kept in large carboys insecurely stoppered, and consequently becomes oxidized by the air and moisture. It should always be purchased in original packages of small size and preserved in a cool, dark place. The acid reaction observed in some samples of spirit of nitrous ether, is due to acetic acid produced by oxidation from the aldehyde always more or less present; such acidity should invariably be neutralized by means of alkali carbonate, before dispensing the spirit in conjunction with alkali iodides, bromides, etc.

Even under the most favorable conditions spirit of nitrous ether gradually deteriorates, and, if found to contain less than 3 per cent. of ethyl nitrite, should be condemned. Exposure to diffused daylight and air accelerates decomposition, hence, when purchased in bulk, drawn from half-filled or carelessly stoppered containers, the spirit is often worthless. The author has repeatedly had occasion to examine the spirit of nitrous ether offered for sale in bulk by jobbers in different parts of the country, and regrets to say that only in a few cases has the strength found ever approached that required by the Pharmacopœia; in some cases, less than 1 per cent. of ethyl nitrite was present.

Amyl Nitrite. Under this name the Pharmacopœia recognizes a liquid containing about 80 per cent. of true amyl nitrite, $C_5H_{11}NO_2$

together with variable quantities of undetermined compounds. Although not a derivative of official alcohol, this preparation may be conveniently considered at this point, owing to its similarity, chemically, to the preceding solution. Amyl nitrite is an ester, or ethereal salt, bearing the same relation to amyl alcohol as ethyl nitrite bears to official or ethyl alcohol. It can be prepared by direct action of nitric acid on purified amyl alcohol, but is now probably altogether obtained by distilling a solution of sodium nitrite with amyl alcohol and sulphuric acid, that portion of the distillate coming over between 95° and 100° C. (203° and 212° F.) being collected, washed with ice-cold sodium carbonate solution, dehydrated with anhydrous potassium carbonate and redistilled below 100° C. (212° F.). According to the equation, $2C_5H_{11}OH + 2NaNO_2 + H_2SO_4 = 2C_5H_{11}NO_2 + Na_2SO_4 + 2H_2O$, 233.56 parts of amyl nitrite should be obtained from 175.62 parts of amyl alcohol, but, in practice, such is not the case.

As amyl nitrite rapidly deteriorates by exposure to air and light, it must be kept in securely closed, small vials, in a dark place. The commercial article is very variable in quality, 16 samples having been examined in 1892 by Dr. C. O. Curtman, with results ranging from 27.14 to 93.71 per cent. of true amyl nitrite. The valuation of amyl nitrite is made gasometrically, as in the case of spirit of nitrous ether, the amyl nitrite being dissolved in a little alcohol previous to introducing it into the nitrometer. The equation, $C_5H_{11}NO_2 + KI + H_2SO_4 = C_5H_{11}OH + I + NO + KHSO_4$, shows that 116.78 Gm. of amyl nitrite will yield 29.97 Gm. of nitric oxide, hence each Cc. of NO at 25° C. (77° F.), weighing 0.00123 Gm., corresponds to 0.004792+ Gm. of $C_5H_{11}NO_2$. In the official test, 0.26 Gm. of amyl nitrite is used, which should yield nearly 43.5 Cc. of nitric oxide at 25° C. (77° F.); for 80 per cent. of 0.26 is 0.208 and $208 \div 0.004792 = 43.4 +$.

PARALDEHYDE. This liquid is a polymeric form of ethylic aldehyde, which latter is an oxidation product of alcohol.

Aldehydes, chemically speaking, are derived from primary alcohols, contain the characteristic group COH, and, upon further oxidation, yield acids. Ethylic or acetic aldehyde, commonly known as aldehyde in commerce, is a colorless, neutral liquid obtained by distilling a mixture of alcohol, water, sulphuric acid and manganese dioxide or potassium dichromate; the crude product is dissolved in ether and charged with ammonia gas. The resulting crystals of aldehyde-ammonia, $C_2H_4ONH_3$, are distilled with diluted sulphuric acid and rectified over calcium chloride. By condensation of three molecules of aldehyde, one of paraldehyde is formed, $3C_2H_4O = C_6H_{12}O_3$.

The latter is usually prepared by passing gaseous hydrochloric acid into aldehyde at ordinary temperature until the liquid is no longer soluble in an equal volume of water. By repeated freezing

and distillation the crude product is purified until it finally all volatilizes at 124° C. (355.2° F.).

CHLOROFORM. Formerly all chloroform was made by distillation of alcohol with a mixture of chlorinated lime and water, and the British Pharmacopœia still recommends this process, with the addition of slaked lime. The reactions by this method are somewhat complicated, resulting in the formation of chloroform and calcium chloride and formate. The distillate is shaken with water to remove any undecomposed alcohol when crude chloroform separates.

Some chloroform is also obtained commercially by treating chloralhydrate with sodium hydroxide when the following reaction occurs: $C_2HCl_3O.H_2O + NaOH = CHCl_3 + NaCHO_2 + H_2O$. The chloroform is distilled off while sodium formate remains in aqueous solution.

Since 1885 nearly all the chloroform has been made from acetone, by distillation with chlorinated lime, it having been found to be the richest chloroform-yielding substance known. Acetone is extensively produced by destructive distillation of acetates or acetic acid (see page 551), and, since calcium acetate is regenerated in the manufacture of chloroform by the acetone process the latter has proven most profitable. A full description of the method and apparatus used can be found in the *American Journal of Pharmacy*, for 1889. The reaction occurring may be illustrated as follows: $2C_3H_6O + 6CaOCl_2 = 2CHCl_3 + Ca(C_2H_3O_2)_2 + 2Ca(OH)_2 + 3CaCl_2$. The chloroform obtained by this method is quite free from the chlorinated by-products frequently found in that made from alcohol.

For the purpose of purification on a commercial scale, chloroform is made to bubble up slowly through two successive deep layers of concentrated sulphuric acid, and afterward brought into intimate contact with anhydrous sodium carbonate for the purpose of removing any water and acid mechanically carried over. Finally the chloroform is siphoned into a dry still and distilled in a water-bath at a temperature not exceeding 62° C. (142.60° F.). The same method slightly modified, so as to adapt it to small quantities, is recommended in the Pharmacopœia for the treatment of chloroform not complying with the official requirements. The sulphuric acid destroys any organic impurities present and gradually darkens in color, becoming finally black.

Absolutely pure chloroform is very unstable when exposed to air and diffused daylight, but if air be rigidly excluded it does not suffer decomposition even in direct sunlight. Experience has proven that the best preservative agent for chloroform is alcohol, and the Pharmacopœia therefore directs the presence of from 0.6 to 1.0 per cent. of the latter. The chief products of decomposition of chloroform are free chlorine and carbonyl chloride, $COCl_2$, which are readily detected by the official tests, and no chloroform should be used for internal administration which shows any contamination. The

present Pharmacopœia recognizes but one kind of chloroform, but the term "purified chloroform" is still used by some manufacturers.

The term formyl terchloride is sometimes applied to chloroform, which indicates its chemical composition, $CHCl_3$, as a haloid ether; it may also be called trichlormethane if looked upon as methane or marshgas in which three hydrogen atoms have been replaced by chlorine.

BROMOFORM or tribromomethane, $CHBr_3$, is a compound analogous to chloroform. It is now chiefly obtained by the action of alkali hyprobromite on acetone in place of alcohol. The reaction, resembling that explained under chloroform, takes place also in the cold, the bromoform separating as a colorless very heavy liquid of 2.9 specific gravity and boiling at 148° C. (298.4° F.). It is sparingly soluble in water but readily so in alcohol, and is easily decomposed by sunlight. Bromoform is unfit for use if colored or of an acid reaction.

ETHYL BROMIDE. This liquid, also known as hydrobromic ether, belongs, like chloroform and bromoform, to the class of compounds called by chemists haloid ethers, one or more atoms of hydrogen in hydrocarbons or of hydroxyl in the corresponding alcohols having been replaced by either of the haloid elements. While not official in the United States and British Pharmacopœias, it is recognized in the German Pharmacopœia as *æther bromatus*, and is prepared by distilling a mixture of potassium bromide, alcohol, and sulphuric acid, washing the distillate with potassium carbonate solution and then water and finally rectifying over calcium chloride. The following equation explains its formation: $C_2H_5OH+KBr+H_2SO_4=C_2H_5Br+KHSO_4+H_2O$. Ethyl bromide is a colorless liquid of nearly the same specific gravity as chloroform, but boiling at 38° or 40° C. (100.4°–104° F.); it has a neutral reaction but is readily decomposed by light and air, becoming acid and dark in color. It must not be confounded with ethylene bromide, $C_2H_4Br_2$, a liquid of 2.163 specific gravity and boiling at 131° C. (267.8°F.).

CHLORAL. It is unfortunate that the Pharmacopœia has continued the blunder of its predecessor by applying the term chloral, as the official title, to the well-known hydrate of that compound, and more particularly since foreign pharmacopœias have recognized the proper name. True chloral is an oily liquid having the composition, C_2HCl_3O, whereas the official article is a crystalline compound of the same with water.

In the manufacture of chloral, perfectly dry chlorine gas is passed into cold absolute alcohol as long as the former continues to be rapidly absorbed, after which the mixture is gradually warmed up to 60°–70° C. (140°–158° F.) and treated with sulphuric acid, whereby crude chloral is separated as a thin oily liquid, which is then rectified over burned lime and chalk; the final distillate of pure chloral is

weighed and hydrated by the addition of a calculated quantity of water, and the hot mass poured upon plates of glass, covered with a bell-glass and allowed to crystallize.

The reactions occurring in the above process were formerly supposed to consist in the formation of aldehyde and the conversion of this into chloral or trichloraldehyde by the action of chlorine, as illustrated by the equations, $C_2H_5OH+Cl_2=C_2H_4O+2HCl$ and $C_2H_4O+Cl_3=C_2HCl_3O+3HCl$. This view is no longer tenable, since it has been found that chlorine brought into contact with aldehyde yields trichlorbutylaldehyde, $C_4H_5Cl_3O$, a condensation product, instead of chloral. According to recent authorities, the nascent aldehyde produced by the action of chlorine on alcohol, acts upon the absolute alcohol present, forming acetal and water, thus: $2C_2H_5OH+C_2H_4O=C_2H_4(OC_2H_5)_2+H_2O$; the acetal is converted by chlorine into trichloracetal, $C_2H_4(OC_2H_5)_2+Cl_6=C_2HCl_3(OC_2H_5)_2+3HCl$, and this is decomposed by the hydrochloric acid present into chloral alcoholate and ethyl chloride, thus $C_2HCl_3(OC_2H_5)_2+HCl=C_2HCl_3O.C_2H_5OH+C_2H_5Cl$; finally the chloral alcoholate is decomposed by sulphuric acid into chloral, ethyl sulphuric acid, and water, $C_2HCl_3O.C_2H_5OH+H_2SO_4=C_2HCl_3O+C_2H_5HSO_4+H_2O$. Other decomposition products are also formed in small quantities.

In order to further purify the crystals of chloral hydrate, it is customary for manufacturers to again decompose the hydrate with sulphuric acid, whereby pure chloral is set free, and then rectify, rehydrate, and recrystallize the product.

Chloral hydrate should never be exposed to direct sunlight and its aqueous solutions, dispensed in conjunction with strongly alcoholic liquid, are apt to separate less soluble chloral alcoholate. When dispensed together with concrete volatile oils or phenols, the mixture should be thoroughly triturated until perfect solution (liquefaction) has been obtained. Mixed with alkalies, chloral is split up into chloroform and alkali formate. (See page 582.)

Chloral has yielded a number of derivative products which are used to some extent. The most prominent of these is chloralamide, $C_2HCl_3O.CHONH_2$, made by interaction between anhydrous chloral and formamide, $CHONH_2$ (a colorless oily liquid produced by dry distillation of urea and ammonium formate), at about 140° C. (284° F.). It is recognized in the German Pharmacopœia as *chloralum formamidatum*, and occurs in white, lustrous crystals which are slowly soluble in cold water but are decomposed by water heated to 60° C. (140° F.). Chloralamide is used as a hypnotic, and must not be confounded with chloralimide obtained by the action of heat on chloral-ammonium.

Other compounds, such as hypnal, a compound of chloral and antipyrine,—somnal, a compound of chloral, urethane, and alcohol—ural or uralium, chloral-urethane—and others are less important. (A full account of these may be found in the *National Dispensatory*, fifth edition, p. 455.)

Closely allied to the official chloral is butyl-chloral hydrate, which is recognized in the British Pharmacopœia, and is, in commerce, often, although wrongly, called croton-chloral hydrate. It is prepared from ethylic aldehyde, by acting upon it with chlorine, at a low temperature——10° C. (14° F.); the mixture is finally subjected to fractional distillation until a product boiling uniformly between 163° and 165° C. (325.4° and 329° F.) is obtained, consisting of trichlorbutylaldehyde or butyl-chloral, which is then converted into the crystalline hydrous variety by addition of water. Butyl-chloral hydrate dissolves sparingly in cold water, but freely in hot water, alcohol, and glycerin. It differs from chloral hydrate by not yielding chloroform with alkalies but instead dichlorallylene, $C_3H_2Cl_2$.

Iodoform. This compound may be obtained from alcohol or acetone, by the action of iodine in the presence of alkali hydroxides or carbonates. For many years only alcohol was used and either Bouchardat's or Filhol's process employed. The former consists in heating iodine, potassium bicarbonate, alcohol, and water, in a long-neck flask, to between 60° and 80° C. (140° and 176° F.), until the color has disappeared, then adding small portions of iodine as long as these are taken up and decolorized; the mixture is finally set aside for twenty-four hours and the crystals collected on a filter. About one-third of the iodine is recovered as iodoform, the remainder forming potassium iodide.

Filhol's process insures a much larger yield. Iodine is added in small portions to a warm mixture of sodium carbonate, water, and alcohol, and, after cooling, the crystals are collected; the filtrate is again warmed, some alkali carbonate added and a rapid current of chlorine passed through the liquid as long as iodoform is separated, which is again collected and the filtrate made to yield more iodoform by repeating the treatment. The formation of iodoform may be illustrated by the following equations $C_2H_5OH+I_8+6KHCO_3=CHI_3+5KI+KCHO_2+6CO_2+5H_2O$, alkali formate being probably always produced together perhaps with ethyl iodide, acetic ether, and other compounds. The results appear to be greatly influenced by the relative proportions of the materials used and the temperature employed.

Since 1889 the process of Sulliot and Raynaud has been largely used, by means of which iodoform of unusual purity is obtained. A solution of fifty parts of sodium or potassium iodide (in France derived from the ash of sea-weed) is mixed with six parts of acetone and a solution of two parts of caustic soda in 1000 parts of water; a dilute solution of sodium hypochlorite is added, drop by drop, as long as iodoform is produced, the yield being about the theoretical quantity according to the equation, $3NaI+3NaClO+C_3H_6O=CHI_3+3NaCl+NaC_2H_3O_2+2NaOH$.

In Germany iodoform has also been made by subjecting a solution of fifty parts of potassium iodide in 300 parts of water and thirty

parts of alcohol to electrolysis while a constant current of carbon dioxide is being passed into the liquid.

During the past ten years several substitutes for iodoform have been introduced, but in spite of the persistent unpleasant odor of the latter its use by physicians still surpasses that of the proposed substitutes, of which the two best known are iodol and aristol. Iodol is chemically tetraiodopyrrol, C_4I_4NH, obtained by the interaction of iodine and pyrrol (a weak base found in coal tar) in alcoholic solution; it falls as a yellowish, flocculent precipitate, upon the addition of water and contains about 89 per cent. of iodine. Aristol, also known as *annidalin*, is chemically dithymoldiiodide, $C_{20}H_{24}O_2I_2$, and is prepared by adding a strong solution of thymol in sodium hydroxide solution, with constant stirring and at an ordinary temperature, to a strong solution of iodine and potassium iodide in water; aristol is formed as a dark brownish-red precipitate, which is subsequently washed with water and dried.

Other compounds which have been recommended as substitutes for iodoform are europhen, or diisobutylorthocresol-diiodide, an amorphous yellow powder, sozoidol or sozoiodolic acid and its salts, occurring in crystalline form, sulphamniol or thioxydiphenylamine, a yellow insoluble powder, losophane or triiodometacresol, odorless and colorless crystals containing nearly 80 per cent. of iodine. The advantage claimed for some of these is the absence of color and odor; a full account of them can be found in the *National Dispensatory*, fifth edition, pp. 879 and 880.

Among the non-official alcohol derivatives may be mentioned the following:

Bromal. CHBrO. This compound resembles chloral in its chemical nature, and, like it, forms a hydrate and an alcoholate. It is prepared, like chloral, from absolute alcohol, by the action of bromine. With alkali hydroxides bromal forms bromoform and alkali formate. It must not be confounded with bromol, which is tribromophenol. (See page 558.)

Urethane. While in chemistry the term urethane is applied to all ethers of carbamic acid, in pharmacy and medicine it is restricted to one compound, namely, ethyl urethane or ethylcarbamate, $CONH_2OC_2H_5$. It can be obtained in several ways, but for medicinal use is prepared by heating in a sealed tube a mixture of urea nitrate and alcohol for several hours at a temperature of 120°–130° C. (248° 266° F.); the resulting crystalline mass is dissolved in water and shaken with ether, which latter extracts the urethane and yields it in crystals, upon distillation, which may be further purified by recrystallization from water. Phenyl urethane is known in commerce as *euphorine*.

SULPHONAL. This is the copyrighted name applied to a definite chemical compound and recognized in the British and German Pharmacopœias. Its chemical formula, $(CH_3)_2C(SO_2C_2H_5)_2$, shows it to be diethylsulphonyl-dimethylmethane. Sulphonal is prepared by oxidation of mercaptol with potassium permanganate and purified by recrystallization from water or alcohol. (Mercaptol is an oily liquid obtained by passing dry hydrochloric acid gas into a mixture of two parts of anhydrous ethyl hydrosulphide or mercaptan and one part of anhydrous acetone.)

TRIONAL is diethylsulphonyl-methylethylmethane, and is prepared exactly like sulphonal except that methyl ethyl ketone is used in place of acetone in the manufacture of mercaptol; if diethyl ketone be used in place of acetone, another compound known as TETRONAL is obtained. All three compounds occur in the form of colorless crystals and are sparingly soluble in cold water.

CHAPTER LVI.

FATS AND FIXED OILS.

THE physical properties of these compounds have already been considered on pages 186–195. Chemically they belong to the class of esters, or ethereal salts, being readily convertible into the respective acids and alcohols by means of alkali hydroxides. With a few exceptions, the basylous radical is the same for all fats and fixed oils, whether obtained from the vegetable or animal kingdom, namely, glyceryl or propenyl, C_3H_5, a trivalent group derived from the hydrocarbon propane, C_3H_8, the alcohol or hydroxide of which is glycerin or propenyl alcohol, $C_3H_5(OH)_3$; other bases obtainable from fats are cholesterin, myricin, cerotin, cetin, etc. The acid radicals found in fats are many, the chief ones being oleic, palmitic, stearic, lauric, arachic, erucic, and myristic acids, varying from one to three or more in number for a single fat or fixed oil.

The ordinary fats and oils used in pharmacy consist, for the most part, of two or three compound ethers, to which the names olein, palmitin, and stearin have been given; of these, olein, being always liquid, naturally forms the chief constituent of fixed oils, while palmitin and stearin, being solid at ordinary temperatures, by their presence determine the firmer consistence of solid fats. All three are fatty acid esters of glyceryl, known respectively to chemists as glyceryl trioleate, $C_3H_5(C_{18}H_{33}O_2)_3$, glyceryl tripalmitate, $C_3H_5(C_{16}H_{31}O_2)_3$, and glyceryl tristearate, $C_3H_5(C_{18}H_{35}O_2)_3$; the names glycerides of oleic, palmitic, and stearic acid are also applied to them. The oleic acid derived from different oils, not having a uniform composition and properties, specific names are employed to distinguish the respective glycerides; thus, olein, $C_3H_5(C_{18}H_{33}O_2)_3$, linolein, $C_3H_2(C_{18}H_{31}O_2)_3$, and physetolein, $C_3H_2(C_{18}H_{29}O_2)_3$; the first named occurs both in animal and vegetable fats, the second only in vegetable fats, while the third is confined to animal fats, chiefly fish oil, seal oil, etc.

The following true fats, recognized in the Pharmacopœia, are mixtures of glyceryl esters:

ANIMAL FATS. *Lard*, composed of about 60 per cent. of olein and 40 per cent. of a mixture of stearin and palmitin. *Lard oil* is almost pure olein with small and varying proportions of palmitin and stearin, dependent upon the care with which the oil has been expressed. *Suet* consists of about 75 or 80 per cent. of stearin and

palmitin and 20 or 25 per cent. of olein. *Codliver oil* contains in its crude state about 70 per cent. of physetolein, 25 per cent. of palmitin together with small quantities of stearin and other glycerides; its acid character is due to the presence of free fatty acids. It is said also to contain organic compounds of iodine, bromine, phosphorus and sulphur, as well as trimethylamine, asellin, $C_{25}H_{34}N_4$?, morrhuin, $C_{19}H_{27}N_3$?, and morrhuic acid, $C_9H_{13}NO_3$? Morrhuol, said to represent the active virtues of codliver oil, is obtained by treating the latter with 90 per cent. alcohol and distilling the liquid after filtration; it constitutes the oily residue left in the still, has a disagreeable odor and a sharp, bitter taste.

VEGETABLE FATS. *Almond oil* (*expressed*) is probably the purest form of olein, containing only very small quantities of the esters of linolic and the solid fatty acids, hence it can be cooled to near —20° C. (—4° F.) without congealing. *Castor oil* consists chiefly of ricinolein, $C_3H_5(C_{18}H_{33}O_3)_3$, which differs from olein in being the glyceride of an acid containing in each molecule one more oxygen atom than oleic acid; small quantities of stearin are also present. It differs from other fixed oils in being readily soluble in alcohol and insoluble in benzin, petroleum, and paraffin oils. *Cottonseed oil* is a mixture of olein, palmitin, and linolein; it contains also a small proportion of a non-saponifiable body. In its crude state the oil contains albuminous and resinous matter, to which latter the dark color is due. *Croton oil* contains olein, palmitin, stearin, and the glycerides of a number of other fatty acids. The vesicating and purgative action of croton oil is, according to the latest investigations of Kobert, due to crotonolic acid, which exists in the oil both in the free state and as a glyceride and can be extracted by means of alcohol. *Linseed oil*, when pure, consists of 80 or 90 per cent. of linolein, the balance being made up of stearin, palmitin, olein, etc. Its property of absorbing oxygen and increasing in weight is explained elsewhere. *Olive oil* is a mixture of about 70 per cent. of olein, 5 per cent. of linolein, and 25 per cent. of palmitin and arachin, the latter two glycerides being present in greater proportion in the lower grades of the oil. The green color is due to chlorophyll in solution. *Sesame oil* contains olein, palmitin, and stearin. *Oil of theobroma*, or *cacao butter*, is composed of the glycerides of oleic, palmitic, stearic, lauric, and arachic acids.

Among the fats used in pharmacy which do not contain the radical glyceryl, the following may be named: *Beeswax*, which consists of myricyl palmitate, $C_{30}H_{61}.C_{16}H_{31}O_2$, and free cerotic acid, $HC_{27}H_{53}O_2$, with small quantities of free melissic acid. *Spermaceti* is chiefly cetyl palmitate, $C_{16}H_{33}C_{16}H_{31}O_{27}$, which, during the life of the sperm whale, is held in solution in sperm oil or cetinelain. *Lanolin* is a mixture of various compound ethers of cholesterin and isocholesterin, $C_{27}H_{45}OH$, the official article containing also 30 per

cent. of water; the cholesteryl esters cannot be saponified by boiling with an aqueous solution of potassa, hence they can be readily separated from other fats and free fatty acids with which they are associated in the grease of sheep's wool. Cholesterin fats are easily distinguished from glycerin fats by the appearance of a pink color, gradually changing to green or blue, when concentrated sulphuric acid is allowed to drop slowly into a solution of 0.1 Gm. of the fat (lanolin) in 3.5 Cc. of acetic anhydride, $(C_2H_3)_2O$; fatty acid glycerides do not show this color reaction.

When absolutely pure, fats and fixed oils are without action on litmus, but in the presence of air, light and moisture, decomposition and oxidation gradually ensue, an unpleasant odor, due to the formation of volatile products, and an acid reaction being observed. Fats are not affected by a temperature of 100° C. (212 F.) but, at 250° C. (482° F.), they are decomposed, various volatile products being formed, among which is an irritating, odorous substance, called acrolein, which, chemically, is allyl aldehyde, C_3H_4O, and is derived from the decomposition of the glycerin present in fats.

The division of fixed oils into drying and non-drying oils has already been mentioned on page 187; to the first class belongs linseed oil, while olive oil and expressed oil of almond are representatives of the second class. A third class might be named, embracing those oils which partake of some of the properties of both the drying and non-drying oils; this class includes castor oil, cottonseed oil, and sesame oil. This difference in their behavior when exposed to air, is due to difference in chemical composition, drying oils being glycerides of linoleic acid, $C_{16}H_{28}O_2$, which, upon exposure to air, absorb oxygen and are converted into oxylinolein, $C_{32}H_{54}O_{11}$, or linoxin. Recent investigations have shown linoleic acid to be a mixture of variable proportions of three other acids beside oleic acid, which former are alone concerned in the gradual solidification of drying oils. The smaller the proportion of oleic acid present in drying oils, the more rapidly and thoroughly will the oil solidify upon exposure; this explains why oils belonging to the same group with cottonseed oil, dry so much more slowly and imperfectly than the members of the linseed oil group. The glyceride of oleic acid present in drying oils behaves like that of the non-drying oils, but decomposition is probably estopped by the formation of the other oxidation products; hence the unpleasant odor and acidity before mentioned are not observable in true drying oils.

Non-drying oils, consisting chiefly of the glyceride of oleic acid, with varying proportions of palmitin, upon exposure to air, appear to absorb water and split up into free oleic (and palmitic) acid and glycerin, the latter being gradually oxidized into carbon dioxide and water, and thus disappearing. The oleic acid absorbs oxygen and is gradually converted into oxystearic acid and finally into volatile odorous acids, such as capronic, valerianic, etc. This process of decomposition is termed rancidification and explains the condition

termed rancidity, noticed in old and carelessly preserved fats and fixed oils. By some it is thought that the change is superinduced by the presence of mucilaginous or albuminous matter in the fat, acting as a ferment under the influence of light, air and moisture. Rancid fats, therefore, always contain free acid and yield less glycerin than sweet fats, when saponified.

In the chemical examination of fats and fixed oils for adulterations, etc., two reactions are especially employed by analysts, namely: that with potassium hydroxide and that with iodine. In the first case 1 or 2 Gm. of the fat or oil are boiled with a definite volume, 25 Cc., of alcoholic solution of potassium hydroxide, of known strength, in a flask in a water-bath until saponification is complete, usually about 15 minutes, and an excess of alkali remains; the excessive alkali is determined volumetrically with deci or semi-normal acid and thus the quantity of alkali used for saponifying the fat ascertained; from this, the number of milligrammes of potassium hydroxide required by one gramme of any fat or fixed oil is calculated, which is called Koettsdorfer's saponification factor of that particular fat or oil.

The iodine test depends upon the fact that fats are capable of combining with varying quantities of iodine and forming colorless addition products under certain favorable conditions. Two solutions are used for this test, which is known as Hübl's iodine test, namely one, consisting of 5 Gm. of iodine in 100 Cc. of 95 per cent. alcohol, and another consisting of 6 Gm. of pure mercuric chloride in 100 Cc. of 95 per cent. alcohol. Equal volumes of the two solutions are mixed and allowed to stand for twenty-four hours in a well-closed bottle, after which the iodine value of the mixture is determined by titration with decinormal sodium thiosulphate solution. The fats or fixed oils are then tested at once, as follows: 0.2 Gm. of drying oils, 0.4 Gm. of non-drying oils, or 0.8 Gm. of solid fats are weighed into a 500 Cc. flask and dissolved in 10 Cc. of chloroform, after which 25 Cc., or in the case of drying oils, 40–60 Cc., of the above iodine mixture are added; if after agitation the liquid is not clear a little more chloroform must be added. The flask is tightly closed and set aside for two hours, when the mixture should still remain highly colored, otherwise 10 or 15 Cc. more of the iodine mixture are added and the flask set aside for two hours more. About 20 Cc. of a 10 per cent. aqueous solution of potassium iodide are now added, as also 150 Cc. of water and decinormal sodium thiosulphate added from a burette, with frequent agitation, until both the aqueous and chloroformic layers are decolorized, using starch mucilage as an indicator toward the end. Having thus ascertained by difference the amount of iodine actually absorbed by the fat, the iodine number, as the amount of iodine absorbed by 100 Gm. of any fat or oil is usually termed, can readily be calculated by the rule of three, thus if 0.4 Gm. of a fixed oil have absorbed or combined with 0.3 Gm. of iodine the iodine number of that oil will be 75 for 0.4 : 0.3 : : 100 : 75.

The following table shows the behavior, when pure, of some of the leading fixed oils used in pharmacy toward potassium hydroxide and iodine. The variations are due to age and other unavoidable conditions :

Name.	Saponification Factor.	Iodine Number.
Expressed Oil of Almond . .	187.9–195.4	97.5– 98.9
Olive Oil	185.2–196.0	81.6– 84.5
Castor Oil	176.0–181.5	86.6– 93.9
Sesame Oil	190.0–194.6	108.9–111.4
Cottonseed Oil	191.0–210.5	110.9–115.7
Linseed Oil	189.0–195.2	155.2–178.5

The action of acids on fats and fixed oils varies considerably; thus, strong hydrochloric acid has no effect upon them, as also cold diluted nitric acid and cold or hot diluted sulphuric acid. Nitrous acid, as well as warm nitric acid, converts olein into elaidin, a compound isomeric with it, but of firm consistence. Strong sulphuric acid decomposes fats slowly in the cold and rapidly with the aid of heat, forming sulpho-compounds of the fatty acids, as well as of the glycerin. If concentrated sulphuric acid be added to almond or olive oil and the mixture be kept at a temperature below 50° C. (122° F.), sulpho-oleic and glyceryl sulphuric acids will be formed, $HSO_3C_{18}H_{33}O_2$ and $C_3H_5(HSO_4)_3$; if castor oil be used, sulphoricinoleic acid will be produced. The glycerylsulphuric acid, upon addition of water, is again converted into glycerin and water, and can thus be removed; the sulpho-oleic acid, having been purified by washing with salt solution, can be combined with alkali hydroxides, yielding water miscible sulpho-oleates, which on account of their absorbability have been recommended as vehicles for ointments, under the names oleite, polysolve, etc. (see page 371).

Decomposition of fats can also be effected by superheated steam, which fact is utilized in the manufacture of glycerin on a large scale, as already explained on page 196.

Saponification. Alkali hydroxides and moist metallic oxides, in the cold, only partly decompose fats and fixed oils, forming emulsions with them, as shown in the case of the official ammonia and lime liniments, but, at boiling temperature, complete dissociation is effected, the fatty acids combining with the metallic base, while glycerin is liberated. The new compounds thus obtained are known as soap, and the process is termed saponification; the character of the soap depends upon the particular hydroxide employed, soda invariably forming hard soap while potassa and ammonia form soft soap. The process of saponification may be illustrated by the following equation, $C_3H_5(C_{18}H_{33}O_2)_3 + 3NaOH = 3NaC_{18}H_{33}O_2 + C_3H_5(OH)_3$, which represents the manufacture of hard soap from olive oil.

In the manufacture of soap it is customary to add the alkali solution in slight excess to the fat, in order to insure complete decomposition of the latter, the excess remaining in solution. Boiling of

the mixture is continued until it becomes transparent and somewhat tenacious, showing that no uncombined fat remains; this is necessary, as the decomposition of the fat is gradual and the newly formed soap serves as an emulsifying agent for the fat. As the process nears completion iridescent bubbles are seen to rise on the surface, consisting of soap solution. Finally common salt is added to the finished solution, whereby the soap is precipitated and can then be drained and allowed to dry in suitable moulds. This explains the fact that ordinary soap will cause no lather with sea water, a special soap made with cocoa-nut oil or resin, and known as *marine soap* being preferable for this purpose, since it is soluble in the solution of salt. Since all fats contain some palmitin or stearin (even the fixed oils), the consistence of the soap will depend in part upon the proportion of solid fats present, being firmest in soaps made partly with stearin fats, such as suet, tallow, etc.

The term saponification is also used to express the decomposition of fats and fixed oils by water with the aid of superheated steam, which results in the liberation of the fatty acids and glycerin, as in the case of tallow or suet, thus: $C_3H_5(C_{18}H_{35}O_2)_3 + 3H_2O = 3HC_{18}H_{35}O_2 + C_3H_5(OH)_3$. Chemists, not confining the process to the glycerides of fatty acids, further apply the term to the resolution of all compound ethers by an alkali into the respective acids and alcohols, which is often practised in connection with the determination of certain constituents of volatile oils. The action of potassa on aldehyde, resulting in the formation of aldehyde-resin, has also sometimes, but erroneously, been called saponification. In pharmacy, the term soap is always restricted to the alkali salts of fatty acids, obtained by treatment of a fat or fixed oil with a boiling solution of soda or potassa, which are soluble in water; the name oleate or plaster is more properly applied to those soaps which are insoluble in water or alcohol and are made with the oxides of the earths or heavy metals. Soap made wholly from animal fat is but sparingly soluble in cold alcohol and therefore to be preferred for the preparation of solid opodeldoc and similar firm liniments.

Medicated Soaps. While soaps intended simply as detergents, may, without detriment, contain a very slight excess of alkali, it is desirable, when medication of the soap is intended, that prior to its application, a perfectly neutral substance be employed; it has, in fact, been found that soap containing uncombined fat is even preferable to neutral or normal soap, for not only does it render the skin softer but reaction between the soap and any medicinal agent added is also thereby avoided or at least retarded. Such soaps, containing an excess of fat, are known as "superfatted soaps" and have been largely used for the past ten years. In preparing them it is customary to add an excess of 3 or 5 per cent. of fat or fixed oil in the beginning of the operation, which then remains intimately mixed with the newly formed soap. In a few cases the excess of fat has been

incorporated with the freshly made, neutral soap while yet in a soft, pasty condition. Both olive oil and lanolin are used in the manufacture of superfatted soaps, having been found preferable to all other fats in their action on the skin and toward chemicals.

In the manufacture of medicated soaps the plan followed is identical with that prescribed on page 373 for ointments. The medicinal agent is first intimately mixed (either in the form of solution or impalpably fine powder) with a small portion of the superfatted soap, by means of suitable apparatus, which mixture is then added to such a further quantity of the same vehicle as may be necessary to establish the required percentage strength of the finished product. Among the various medications of superfatted soaps are tar 5 per cent., sulphur 10 per cent., salicylic acid 5 per cent., borax 5 per cent., carbolic acid 5 and 10 per cent., corrosive sublimate $\frac{1}{10}$ and $\frac{1}{2}$ per cent., camphor 5 per cent., and others.

Official Soaps. The Pharmacopœia recognizes two varieties of soap, one by the general name *soap* (Latin, *sapo*) and the other by the general name *soft soap* (Latin, *sapo mollis*). The first is intended to be a hard soap made from olive oil and soda, as already explained. When fresh, or if kept in a damp cellar, it usually contains a large proportion of water, most of which is lost by drying in a warm, airy room and all of which can be expelled at a temperature of 110° C. (230° F.). White castile soap, the kind officially recognized, usually contains a slight excess of alkali, which should not, however, exceed 1 per cent. of sodium carbonate or 0.25 per cent. of sodium hydroxide, as indicated by the official test with $\frac{N}{10}$ oxalic acid solution. The Pharmacopœia also demands the absence of more than 2 per cent. of matter insoluble in water.

The soft soap of the Pharmacopœia is directed to be made by the action of potassa on linseed oil. Commercially, it is generally known as green soap, which was formerly also the official title; the color is, however, by no means green, being yellowish-brown. On account of the unsightly appearance and disagreeable odor of the official preparation, the use of olive in place of linseed oil has been recommended, yielding a more satisfactory product. The value of the official soft soap is partly due to its greater alkalinity. In the German Pharmacopœia this soap is known as *sapo kalinus*.

Lead plaster is sometimes spoken of as lead soap, and, in its manufacture, a process similar to that used for the official hard soap is employed, finely divided lead oxide being allowed to act upon heated olive oil, in the presence of water, forming lead oleate (oleopalmitate) and liberating glycerin, which latter is removed by subsequent washing with warm water. The use of water is essential, as it not only keeps the temperature down to that of boiling water, thus preventing decomposition of the olive oil at a higher heat, but also very materially aids in the reaction between the oil and lead oxide, as shown by the equation, $2C_3H_5(C_{18}H_{33}O_2)_3 + 3PbO + 3H_2O =$

$3Pb(C_{18}H_{33}O_2)_2 + 2C_3H_5(OH)_3$. The finished product, which is a normal lead oleate mixed with small quantities of lead palmitate, owing to the palmitin in the olive oil, should not be sticky or greasy to the touch, and should dissolve completely in warm oil or turpentine, showing the absence of free oil and uncombined lead oxide.

The name diachylon plaster, which is still applied to lead plaster, was given to it during the middle ages, when mucilage of linseed, althæa and similar substances, was added to the mixture before heating, with the view of retarding the evaporation of water and possibly also to increase the plastic condition of the finished product. The term diachylon is derived from the Greek words *διά*, through or with, and *χυλός*, juice.

GLYCERIN. As already stated, the basylous radical found in nearly all fats and fixed oils is glyceryl, the hydroxide of which is glycerin, $C_3H_5(OH)_3$, a triatomic alcohol. Its manufacture, on a commercial scale, has been explained on page 195. While glycerin is unaffected by cold nitric or sulphuric acid separately, a mixture of the two acids forms with it a definite chemical compound, glyceryl or propenyl trinitrate, $C_3H_5(NO_3)_3$, commonly but wrongly called nitroglycerin and also known as glonoin and trinitrin.

Glyceryl trinitrate is prepared by adding a mixture of 100 parts of anhydrous glycerin and 3 parts of sulphuric acid spec. grav. 1.835, gradually and in small portions at a time, to a well-chilled mixture of 280 parts of nitric acid spec. grav. 1.5, and 300 parts of sulphuric acid spec. grav. 1.835, the vessel being kept surrounded by ice. This mixture is afterward poured into six times its volume of cold water, washed free from acid, and finally dried over sulphuric acid. The reaction may be illustrated as follows: $C_3H_5(OH)_3 + 3HNO_3 + H_2SO_4 = C_3H_5(NO_3)_3 + 3H_2O + H_2SO_4$, the sulphuric acid simply serving to withdraw the water eliminated in the formation of the compound ether.

The product is a slightly yellowish, oily liquid, insoluble in water but soluble in alcohol. It has a sweet, aromatic taste, and is very poisonous.

In the form of a 1 per cent. alcoholic solution, glyceryl trinitrate is recognized, in the Pharmacopœia, as *Spirit of Glonoin;* tablet triturates and chocolate tablets containing 0.00065 and 0.0013 Gm. ($\frac{1}{100}$ and $\frac{1}{50}$ grain) of glonoin each are also used by physicians; mixed with three parts of infusorial earth (kieselguhr), it constitutes dynamite, a well-known blasting agent.

PETROLEUM PRODUCTS. Pharmaceutically closely allied to the fats, but chemically entirely distinct are those mixtures of hydrocarbons of the paraffin series obtained by purification of the residuum from the distillation of American petroleum. They are recognized in the Pharmacopœia by the name "Petrolatum," in three varieties, as liquid, soft, and hard; a still firmer variety is recognized

in the British and German Pharmacopœias as "hard paraffin." These substances are fat-like in appearance and extensively employed as vehicles for the application of numerous remedial agents; commercially they are known as vaseline, cosmoline, albolene, petrolina, etc.

The existence of petroleum in the earth has not as yet been satisfactorily explained; several theories have been advanced, the most acceptable of which is that petroleum is the result of dissociation of large quantities of fatty matter (derived from marine animals), while under long-continued pressure, at a moderate temperature, with entire exclusion of air.

American petroleum consists of a mixture of hydrocarbons of the fatty or marsh gas series from methane upward to those richest in carbon, together with small and varying proportions of aromatic hydrocarbons. Upon subjecting the crude petroleum to a refining process by fractional distillation, benzin or naphtha, illuminating oils, and a residuum largely composed of paraffins are obtained. All fractions are then further purified by treatment with sulphuric acid and subsequently with alkalies, after which they are subjected to further fractional distillation. The benzin recognized in the Pharmacopœia also as petroleum benzin or petroleum ether, is collected between 50° and 60° C. (122° and 140° F.) and should be free from sulphur compounds. Its chief components are the hydrocarbons, pentane (C_5H_{12}), and hexane (C_6H_{14}). Official benzin is a valuable solvent for fats, caoutchouc, and some alkaloids, and, as such, is extensively employed; it must not be confounded with benzene, C_6H_6, a coal tar derivative (see page 555). Benzin is highly inflammable, and its vapor, like that of ether, is explosive when mixed with air and ignited.

Upon distilling the purified residuum from the crude petroleum at higher temperatures, "paraffin oils" are obtained together with a residue of pitch. These paraffin oils are filtered, while hot, through freshly burned bone-black, for the purpose of removing odor and color, and then subjected to distillation until the desired consistence or melting-point of the residuary portion is obtained. The three official varieties of petrolatum differ from each other simply in the graded removal of lower hydrocarbons.

Petrolatum is not saponifiable and not subject to rancidity. If properly purified, it consists only of hydrocarbons, which are not affected at all by cold acids and alkalies and only slightly by hot acids; hence the name paraffins has been given to the products, from the words *parum*, too little, and *affinis*, allied, on account of their lack of affinity for other substances.

Hard paraffin is obtained partly as a residue from the above-mentioned paraffin oils and also largely by the purification with sulphuric acid, etc., of ozokerite or mineral (earth) wax. It occurs as a white, crystalline, odorless, wax-like body, having a melting-point varying from 65° to 80° C. (149°–174° F.), according to its source. Ceresin is a yellow variety of purified earth wax, often used to adulterate yellow beeswax.

CHAPTER LVII.

VOLATILE OILS AND RESINS.

VOLATILE oils form a very important class of pharmaceutical plant products. Their physical properties and the mode of obtaining them have already been fully considered on pages 196–204. Chemically, volatile oils differ radically from fats and fixed oils, as they are not capable of saponification and contain no glycerin. Moreover, by exposure to air, they undergo resinification, but do not become rancid. They may be said to consist of hydrocarbons of the aromatic series, usually associated with oxygen derivatives, alcohols, aldehydes, compound ethers, acids, ketones, and phenols. While some volatile oils are complex mixtures, others are of very simple composition. The hydrocarbons found in volatile oils all belong to one of the following groups: terpenes of the composition $C_{10}H_{16}$, which include pinene, camphene, dextrorotatory limonene (known also as hesperidine, citrene, or carvene), lævorotatory limonene, dipentene or cinene, sylvestrene, and phellandrene; sesquiterpenes of the composition $C_{15}H_{24}$; diterpenes of the composition $C_{20}H_{32}$; polyterpenes of the composition $(C_{10}H_{16})_x$

Chemists must rely largely upon fractional distillation for separation of the different constituents, in addition to which the examination of volatile oils is materially aided by determination of their optical rotation by means of the polariscope, as explained on pages 512–514 of the Pharmacopœia.

The behavior of volatile oils with acids, alkalies, and other reagents must naturally vary greatly, owing to the diversity in their constitution. Those oils composed almost wholly of terpenes form either solid or liquid compounds with hydrochloric acid. Other oils are oxidized and converted into resin-like bodies by nitric acid, while sulphuric acid thickens some volatile oils and completely chars others. Color reactions also occur between some of the oils and sulphuric and other acids. Alkali carbonates are without much effect on volatile oils unless the latter contain acids, but alkali hydroxides, in both aqueous and alcoholic solution, are more active, removing phenols, saponifying compound ethers, etc. Acid alkali sulphites, when added to volatile oils containing aldehydes, combine with the latter to form crystalline compounds. Iodine reacts violently with some oils, and bromine forms crystallizable tetrabromides with others.

The study of the chemistry of volatile oils is a very comprehensive subject, and, while a full treatment thereof cannot be attempted

in this book, the pharmacist of to-day should at least be made familiar with the constituents of the official volatile oils, as shown by investigations made during the past decade, whereby our knowledge of the subject has been so greatly enriched. The *Descriptive Catalogue of Essential Oils*, compiled by Dr. F. B. Power, 1894, gives probably the most complete information to be had in the English language, at the present time, regarding recent determinations of the composition of volatile oils. (The author is indebted to this publication for many valuable data, abstracted by permission of the compiler.)

The Official Volatile Oils.

Oil of Anise. The chief constituent of this oil, 90 per cent. and over, is anethol, $C_6H_4OCH_3C_3H_5$, which solidifies at low temperatures and is accompanied by an undetermined liquid portion, probably a terpene.

Oil of Bergamot. The constituents of this oil are the terpenes, limonene, and dipentene, an alcohol, linalool, $C_{10}H_{17}OH$, and an ester, linaloyl acetate, also known as bergamiol, $C_{10}H_{17}C_2H_3O_2$. This ester is usually present to the extent of 36–39 per cent., and upon it depends the value of the oil; it is determined quantitatively by saponification with sodium hydroxide, as in the case of other compound ethers.

Oil of Betula, also known as oil of sweet birch, constitutes probably the bulk of the commercial oil of wintergreen. Very recent investigations (September, 1895), made by Power and Kleber, have shown that oil of sweet birch, in its unrectified state, contains about 99.8 per cent. of methyl salicylate, together with a very small amount of a paraffin, triacontan, $C_{30}H_{62}$, an aldehyde or ketone, and the ester, $C_{14}H_{24}O_{27}$; it does not, however, contain the alcohol $C_8H_{16}O$, found in oil of gaultheria. The oil is always optically inactive, and, when rectified, would approximate so closely to pure methyl salicylate in composition as to be practically identical with it. The specific gravity of oil of sweet birch is identical with that of the natural oil of wintergreen and like the latter the oil forms a clear solution with five times its volume of 70 per cent. alcohol at a temperature of 20°–25° C. (68°–77° F.).

Empyreumatic oil of birch, known commercially as *oleum rusci* and also as *oleum betulinum* or *oleum muscoviticum*, is obtained by distillation of birch tar or *daggett*, derived by destructive distillation from the wood of the common European birch, betula alba. The oil is of dark brown-red color, having a peculiar penetrating odor like that of Russia leather, and somewhat resembles oil of cade in its medicinal properties.

Oil of Bitter Almond. This oil consists of benzoic aldehyde, C_6H_5COH, with variable proportions of hydrocyanic acid. It does not pre-exist in the seed, but is produced from amygdalin (see

glucosides) by fermentation set up in the presence of water, thus, $C_{20}H_{27}NO_{11}+2H_2O=C_6H_5COH+HCN+2C_6H_{12}O_6$. Exposed to the air, the oil is oxidized to benzoic acid, $C_7H_6O_2$, which occurs more rapidly in the absence of hydrocyanic acid. The official test for other volatile oils and nitrobenzene depends upon the removal of the benzoic aldehyde by means of acid sodium sulphite, forming the compound $C_7H_5COH.NaHSO_3$, which enters into solution by the aid of heat. Synthetic oil of bitter almond, made from toluene and purified with acid sodium sulphite, is now extensively sold.

Oil of Cade, obtained by destructive distillation of the wood of the prickly cedar, a species of juniper indigenous to the southern part of France, is also known as *empyreumatic oil of juniper*, and consists of a sesquiterpene, cadinene, $C_{15}H_{24}$, and a mixture of undetermined phenols.

Oil of Cajuput. The chief constituents are a neutral body, cineol or eucalyptol, $C_{10}H_{18}O$ (about 67 per cent.), an alcohol, terpineol, $C_{10}H_{17}OH$, and undetermined terpenes. The commercial article owes its green color to copper, as may be shown by the official test; when redistilled the oil is colorless.

Oil of Caraway is composed of a terpene, limonene, $C_{10}H_{16}$, and a ketone, carvol, $C_{10}H_{14}O$; both compounds are dextrorotatory and are present in proportions varying from 35 to 50 of the former to 65 to 50 of the latter.

Oil of Chenopodium, also known as oil of wormseed, is said to contain a terpene, $C_{10}H_{16}$, and an oxidized body, $C_{10}H_{16}O$.

Oil of Cinnamon. Ordinary oil of Chinese cinnamon, usually designated as *oil of cassia*, is the kind recognized in the Pharmacopœia. It consists chiefly of cinnamic aldehyde, C_8H_7COH, with some cinnamyl acetate, $C_9H_9.C_2H_3O_2$, and small amounts of cinnamic acid, $C_8H_8O_2$. The value of this oil, which is subject to adulteration, may be determined by means of a concentrated solution of acid sodium sulphite, the cinnamic aldehyde uniting with the alkali salt, leaving the other constituents intact; the oil should lose at least three-fourths of its volume by this treatment, showing the presence of 75 per cent. of the aldehyde. A characteristic reaction of oil of cinnamon is the formation of a crystalline compound with nitric acid when equal volumes of the oil and acid are mixed at 0° C. (32° F.); the product is an addition-compound of cinnamic aldehyde and nitric acid, $C_8H_7COHHNO_3$. Oil of Ceylon cinnamon, which has a finer aroma than the official oil, contains, besides cinnamic aldehyde, some eugenol and phellandrene.

Oil of Cloves. The chief constituent of this oil is eugenol, $C_6H_3.C_3H_5.OCH_3.OH$, a monatomic phenol, which is present in prime oil to the extent of from 80 to 90 per cent. and over; besides this, the oil also contains a sesquiterpene, $C_{15}H_{24}$, called caryophyllene. The reaction with potassium hydroxide or ammonia, mentioned in the Pharmacopœia, depends upon the formation of potassium or ammonium eugenol, $C_{10}H_{11}O.OK$ or $C_{10}H_{11}O.ONH_4$. The value of oil of

cloves lies wholly in the eugenol present, hence the quantitative determination of this body is the best method for valuation of the oil. By converting the eugenol into crystalline benzoyl eugenol, $C_{10}H_{11}OC_6H_5CO_2$, by means of benzoyl chloride, C_6H_5COCl, as suggested by Thoms (see *Amer. Journal Pharm.*, 1892, p. 508), the percentage of eugenol in any sample of oil may be calculated from the weight of the new compound obtained.

Oil of Copaiba consists chiefly of a sesquiterpene, $C_{15}H_{24}$, identical with that found in cloves and known as caryophyllene. It is readily oxidized by exposure to air.

Oil of Coriander is composed of a terpene, pinene, $C_{10}H_{16}$, and an alcohol, linalool, $C_{10}H_{17}OH$.

Oil of Cubeb. The composition of this oil varies somewhat with age. Recent oil, distilled from fresh fruit, consists chiefly of a sesquiterpene, cadinene, $C_{15}H_{24}$, with some dipentene, $C_{10}H_{16}$, but, if old or obtained from old fruit, cubeb camphor, $C_{15}H_{24}.H_2O$, is also present.

Oil of Erigeron, better known as oil of fleabane, consists chiefly of dextrorotatory limonene, $C_{10}H_{16}$, together with an undetermined substance readily decomposed by heat.

Oil of Eucalyptus. The composition of this oil depends largely on its source. The oils of Eucalyptus globulus and E. oleosa, which are specially mentioned in the Pharmacopœia, consist chiefly of cineol or eucalyptol, $C_{10}H_{18}O$, a neutral body, to which they owe their medicinal and antiseptic virtues; the first named oil contains also pinene and small amounts of various aldehydes, while the last named contains an aldehyde known as cuminol, $C_9H_{11}.COH$. The official test for the presence of considerable quantities of phellandrene, depending upon the formation of crystalline phellandrene nitrite, $C_{10}H_{16}N_2O_3$, can be made more delicate, according to Power, by mixing the oil first with 5 Cc. of petroleum benzin, then adding the sodium nitrite solution, and lastly the glacial acetic acid, drop by drop, with vigorous agitation after each addition. Some eucalyptus oils contain also citral $C_{10}H_{16}O$, citronellal, $C_{10}H_{18}O$, and geraniol, $C_{10}H_{17}OH$.

Oil of Fennel. This oil contains the terpenes, pinene, phellandrene, and dipentene, together with fenchone, $C_{10}H_{16}O$, and anethol, $C_{10}H_{12}O$; the latter is usually present to the extent of more than 50 per cent. and separates in crystals upon a reduction of the temperature, hence the higher the temperature at which this occurs, the better the oil.

Oil of Gaultheria. The true oil contains, according to Power and Kleber (September, 1895), about 99 per cent. of methyl salicylate, together with a small amount of a paraffin, probably triacontan, $C_{30}H_{62}$, an aldehyde or ketone, an apparently secondary alcohol, $C_8H_{16}O$, and an ester $C_{14}H_{24}O_2$, thus resembling oil of sweet birch very closely in composition. It has a specific gravity of from 1.180 to 1.187 at 15° C. (59° F.), and yields a clear solution when mixed with five times its volume of 70 per cent. alcohol at a temperature of

from 20° to 25° C. (68°–77° F.). Neither oil of gaultheria nor oil of sweet birch contains any trace of benzoic acid or its esters, nor does either oil contain any terpene or sesquiterpene, as was at one time supposed.

Pure fresh oil of wintergreen (gaultheria) always deviates a ray of polarized light to the left, and this deflection should not be less than —0° 25′ in a 100 Mm. tube.

Oil of Hedeoma. According to Kremers, this oil contains pulegone, $C_{10}H_{16}O$, and two ketones of the composition $C_{10}H_{18}O$, which are looked upon as reduction-products of the former body. Formic and acetic acids are also present. Commercially this oil is known as oil of pennyroyal.

Oil of Juniper consists chiefly of pinene with some cadinene, $C_{15}H_{24}$, and a body, as yet undetermined, to which the peculiar odor and taste of the oil are due. The oil obtained from the fruit only should be used in pharmacy.

Oil of Lavender Flowers. This oil contains two alcohols, linalool, $C_{10}H_{17}OH$, and geraniol, $C_{10}H_{17}OH$, a compound ether, linaloyl acetate, $C_{10}H_{17}C_2H_3O_2$, and some cineol. The value of the oil resides in the compound ether, which is present to the extent of 30 or 36 per cent., and may be determined by saponification with sodium hydroxide.

Oil of Lemon contains dextrorotatory limonene, some pinene, and 7 to 8 per cent. of an aldehyde, citral, $C_{10}H_{16}O$, to which the characteristic odor of the oil is due; a small amount of citronellal, $C_{10}H_{18}O$, is also present.

Oil of Mustard, Volatile. Like oil of bitter almond, this oil does not pre-exist in the plant; it is obtained by macerating crushed black mustard seed, after the removal of fixed oil by expression, with water, when a reaction sets in between sinigrin, a glucoside, and myrosin, an albuminoid body. Sinigrin is, chemically, potassium myronate, $C_{10}H_{18}NS_2KO_{10}$, which, under the influence of the albuminoid ferment, is split up into allyl isosulphocyanate, acid potassium sulphate, and glucose, thus: $C_{10}H_{18}NS_2KO_{10}=C_3H_5CSN$ (volatile oil of mustard)$+KHSO_4+C_6H_{12}O_6$. Since the albuminoid myrosin is rendered inert at a temperature between 60° and 70° C. (140° and 158° F.), mustard which has been heated to this point will not yield the volatile oil, nor can hot water be employed in its manufacture; for the same reason, mustard plasters should never be dipped into water that is more than lukewarm.

Volatile oil of mustard always contains traces of carbon disulphide. It has been prepared synthetically by decomposing allyl iodide, C_3H_5I, by means of potassium sulphocyanate in alcoholic solution.

White mustard seed does not yield volatile oil of mustard, since it does not contain sinigrin, but instead sinalbin, having the composition, $C_{30}H_{44}N_2S_2O_{16}$. When sinalbin reacts with myrosin in the presence of water, a very active, oily but non-volatile principle, to which the

name acrinyl sulphocyanate, $C_7H_7O.CSN$, has been given, is formed, together with acid sinapine sulphate, $(C_{16}H_{23}NO_5)H_2SO_4$, and glucose, $C_6H_{12}O_6$.

The official method of valuation depends upon the formation of a crystalline compound, thiosinamine, by the action of ammonia on the oil of mustard, thus: $C_3H_5CSN+NH_3=C_3H_5.CSN_2H_3$. Since 98.87 parts of the oil yield 115.88 parts of thiosinamine, 3 Gm. cannot yield more than 3.51 Gm.

Oil of Myrcia. A complete analysis of this oil, also known as *oil of bay*, recently made by Power (March, 1895), has shown it to be of rather complex composition, containing two terpenes, myrcene, $C_{10}H_{16}$, and phellandrene, $C_{10}H_{16}$, two phenols, eugenol, $C_6H_4C_3H_5.OCH_3.OH$, and chavicol, $C_6H_4C_3H_5OH$, methyl-eugenol, $C_6H_4C_3H_5(OCH_3)_2$, methyl-chavicol, $C_6H_4C_3H_5OCH_3$, and one aldehyde, citral, $C_{10}H_{16}O$. The chief constituents are eugenol and myrcene; the latter is very unstable and readily changed into the polymeric diterpene $C_{20}H_{32}$, which explains the incomplete solution of the oil in alcohol, except in the case of freshly distilled oil.

Oil of Nutmeg consists chiefly of pinene with probably some dipentine; it contains also myristicol, $C_{10}H_{16}O$, and myristicin, $C_{12}H_{14}O_3$.

Oil of Orange Flowers, also known as *oil of neroli*, is said to consist of 40 per cent. of nerolyl acetate, $C_{10}H_{17}C_2H_3O$, 30 per cent. of a lævorotatory alcohol, nerolol, $C_{10}H_{17}OH$, 20 per cent. of limonene and some geraniol.

Oil of Orange Peel. Both the oil derived from the peel of bitter orange and that derived from the sweet orange are officially recognized and show the same specific gravity and optical rotation. They consist chiefly of limonene with small proportions of citral and a lower boiling aldehyde.

Oil of Peppermint. There is probably no volatile oil used in pharmacy of which a greater variety is offered for sale; besides five or six different brands of American oil, oils distilled from English, German, and Japanese peppermint herb are also on the market. Oil of peppermint shows a greater complexity in composition than any other volatile oil known, a recent analysis (1894) by Power and Kleber of average American oil having developed the following constituents, fifteen in number: Acetaldehyde, C_2H_4O; acetic acid, $HC_2H_3O_2$; iso-valeraldehyde, $C_5H_{10}O$; iso-valerianic acid, $HC_5H_{10}O_2$; three isomeric terpenes, pinene, phellandrene, and limonene, $C_{10}H_{16}$; cineol or eucalyptol, $C_{10}H_{18}O$; menthone—a ketone—$C_{10}H_{18}O$; menthol, $C_{10}H_{19}OH$; two compound ethers, menthyl acetate, $C_{10}H_{19}C_2H_3O_2$, and menthyl iso-valeriante, $C_{10}H_{19}C_5H_{10}O_2$; a sesquiterpene, cadinene, $C_{15}H_{24}$; and a lactone of the composition $C_{10}H_{16}O_2$.

The most important constituent is menthol, of which good oil should contain at least 50 per cent., partly in a free state and partly in the form of esters; such oil will readily respond to the official test in a freezing mixture. Japanese oil of peppermint, although rich in menthol (sometimes containing 79 per cent.), is not used medicinally, on account of its peculiar bitter and disagreeable taste.

Oil of peppermint differs from other oils in the variety of its color-reactions with acids, as mentioned in the Pharmacopœia.

Oil of Pimenta or *Oil of Allspice* closely resembles oil of cloves in its constitution, but has a lower specific gravity. It contains eugenol, $C_6H_3C_3H_5.OCH_3OH$, and a sesquiterpene, $C_{15}H_{24}$.

Oil of Rose. This oil shows a marked difference in constitution from other volatile oils, in that the solid crystallizable portion consists solely of a mixture of odorless hydrocarbons, one of which has the composition $C_{20}H_{42}$. The liquid portion of the oil, upon which its fragrance depends, is a mixture of geraniol, $C_{10}H_{17}OH$, with a small quantity of one or more undetermined substances of honey-like odor; it has been called rhodinol. The test given in the Pharmacopœia for the presence in oil of rose of Turkish oil of geranium and oil of rose geranium, can be made more effective by using 5 Cc. of alcohol instead of 2 Cc., as officially directed.

Oil of Rosemary is composed of pinene, cineol, $C_{10}H_{18}O$, borneol, $C_{10}H_{17}OH$, and camphor, $C_{10}H_{17}OH$. The finest commercial variety is that distilled from the flowers and known as the "Eperlé" brand.

Oil of Santal. The official or East Indian oil of sandalwood is said to contain a body called santalal, $C_{15}H_{24}O$, and an alcoholic substance, santalol, $C_{15}H_{26}O$, boiling at 300° C. (572° F.) and 310° C. (590° F.) respectively. Inferior oils, produced in Australia and the West Indies, are all dextrorotatory, while the official oil is lævorotatory. Oil of cedarwood and fatty oils are readily detected by imperfect solubility of the oil in ten volumes of 70 per cent. alcohol. lev.

Oil of Sassafras consists chiefly of safrol, $C_{10}H_{10}O_2$, with a very small amount of eugenol and a dextrorotatory hydrocarbon, $C_{10}H_{16}$, called safrene, probably identical with pinene. Safrol, at ordinary temperatures, is a perfectly colorless liquid of 1.108 specific gravity at 15° C. (59° F.); it is also found in Japanese camphor oil, from which it is now largely obtained. Commercial artificial oil of sassafras is not a synthetic product, but probably made from camphor oil. dex

Oil of Savin contains pinene and the sesquiterpene, cadinene, $C_{15}H_{24}$.

Oil of Spearmint differs radically in its composition from oil of peppermint, containing lævorotatory limonene and lævorotatory carvol, $C_{10}H_{14}O$, with possibly some lævorotatory pinene. lev.

Oil of Tar. This oil, formed during the dry distillation of wood, is obtained from pine tar by fractional distillation. It is a complex mixture of hydrocarbons, acetic and other acids, and undetermined empyreumatic products.

Oil of Thyme. The most important constituent of this oil is thymol, $C_{10}H_{13}OH$, a monatomic phenol; the hydrocarbon cymene, $C_{10}H_{14}$, is also present, as well as very small quantities of bornyl esters. In some oils, thymol is entirely replaced by its isomer, carvacrol, whilst in others, both phenols are found present in equal amounts.

Oil of Turpentine. The official oil, derived from American turpentine, consists almost wholly of dextrorotatory pinene, which, in the crude oil, is associated with resin and other oxidation-products depending upon age and exposure. These impurities, being removable by treatment with lime water and subsequent distillation, are therefore not present in the official *rectified* oil, which alone should be employed for internal use.

Oil of Wintergreen, Synthetic or Artificial. This compound is recognized in the Pharmacopœia as Methyl Salicylate, which name at once indicates its true chemical character, a compound ether. It may be prepared by distilling a mixture of salicylic acid, methyl alcohol, and sulphuric acid, when the following reaction occurs, $HC_7H_5O_3 + CH_3OH + H_2SO_4 = CH_3C_7H_5O_3 + H_2O + H_2SO_4$, methyl salicylate being volatized and condensed in suitable receivers, while diluted sulphuric acid remains in the still. For the purpose of purification, the product is thoroughly washed with water, decanted, and redistilled.

The quality of this oil, as well as that of the oils of betula and gaultheria, is ascertained by means of decomposition with sodium hydroxide, as directed in the Pharmacopœia. Sodium salicylate and methyl alcohol are formed according to the following equation, $CH_3C_7H_5O_3 + NaOH = NaC_7H_5O_3 + CH_3OH$, the former dissolving upon application of heat and subsequently yielding a precipitate of salicylic acid upon supersaturation with hydrochloric acid.

Derivatives of Volatile Oils. The Pharmacopœia recognizes several compounds which, being obtained directly from volatile oils, should be considered at this point.

Camphor. This term is applied to compounds having the composition $C_{10}H_{16}O$, which occur in a number of essential oils and are solid at ordinary temperature. They are no doubt the result of oxidation of hydrocarbons in the plant, and stand in the relation of a ketone to the alcohol borneol, $C_{10}H_{17}OH$. Official camphor is derived solely from the wood of the camphor tree of China and Japan. When camphor wood is heated in the stills the camphor volatilizes and sublimes in the form of small grains which come to this country as crude camphor. It is accompanied, as a by-product, by *oil of camphor*, a liquid of complex composition, containing not less than four hydrocarbons, pinene, phellandrene, dipentene, and cadinene, besides five oxidized bodies, cineol, camphor, terpineol, safrol, and eugenol.

The term *artificial camphor* has been given by some to terpin hydrate, but it is generally applied to terpene hydrochloride, $C_{10}H_{16}HCl$, obtained by saturating oil of turpentine, dissolved in twice its volume of carbon disulphide, with dry hydrochloric acid gas. The compound forms a white, plastic, crystalline mass, melting at 125° C. (257° F.) and possessing the odor and appearance of ordinary camphor. If terpene hydrochloride be heated with potas-

sium stearate in a sealed tube, solid terecamphene, $C_{10}H_{16}$, is formed, which, when boiled with potassium dichromate and dilute sulphuric acid, takes up oxygen and is converted into camphor, $C_{10}H_{16}O$.

Menthol, $C_{10}H_{19}OH$. This body, forming the chief constituent of oil of peppermint, is obtained now almost altogether from the Japanese oil, by simple refrigeration, and is then purified by recrystallization. Its chemical character is that of a secondary alcohol, yielding by moderate oxidation with potassium dichromate and sulphuric acid a ketone, *menthone*, $C_{10}H_{18}O$, and combining with organic acids to form compound ethers, such as menthyl acetate, benzoate, butyrate, formate, etc. By means of dehydrating agents, menthol is converted into the hydrocarbons menthene and dimenthene.

Monobromated Camphor. This compound is obtained by heating camphor and bromine together in a flask or retort (preferably with the addition of water or chloroform) until reaction ceases, then allowing the yellowish solution to crystallize, heating until the mass becomes white, and recrystallizing from alcohol or benzin. The reaction involves the formation of camphor dibromide, $C_{10}H_{16}OBr_2$, which splits up into camphor monobromide and hydrobromic acid, $C_{10}H_{16}OBr_2 = C_{10}H_{15}BrO + HBr$, the latter distilling over with the water or chloroform.

Terebene. This preparation is obtained by the action of concentrated sulphuric acid on oil of turpentine, the acid being gradually added to the oil; the mixture is allowed to stand for a day, after which the supernatant layer is removed, neutralized with chalk, and distilled. Careful investigations by Power and Kleber (1894) have shown that the statements in the Pharmacopœia regarding terebene are erroneous, and that, in its chemical properties, it does *not* resemble oil of turpentine. While the latter oil, as before stated, consists almost wholly of dextrorotatory pinene, true terebene consists chiefly of the hydrocarbons dipentene and terpinene, with some cymol and camphene, and is optically perfectly inactive; the latter is an important test for the presence of unaltered oil of turpentine. The specific gravity of terebene is about 0.855 instead of 0.862 at 15° C. (59° F.) and its boiling point between 170° and 185° C. (338° and 365° F.) instead of 156°–160° C. (312.8°–320° F.).

Terpin Hydrate, $C_{10}H_{18}(OH)_2 + H_2O$. This compound may be obtained by allowing a mixture of four parts of rectified oil of turpentine, 3 parts of 80 per cent. alcohol, and 1 part of nitric acid to stand in large, shallow dishes for several days; the crystals which have separated may then be drained, dried between filter paper, and recrystallized from 95 per cent. alcohol rendered slightly alkaline to remove adhering acid. The yield is about 12 per cent. of the weight of the oil of turpentine used, and the operation should always be performed in the cold, as, during hot weather, resinification of the oil will occur in place of the formation of crystals. Terpin hydrate, when fused or rendered anhydrous over sulphuric acid, yields terpin, $C_{10}H_{18}(OH)_2$, a diatomic alcohol, which, when distilled with moder-

ately dilute sulphuric acid, loses water and is changed chiefly into terpineol, $C_{10}H_{17}OH$, a substance largely employed in perfumery on account of its very fragrant odor, resembling that of fresh lilacs.

Thymol, $C_{10}H_{14}O$ or $C_6H_3.CH_3.C_3H_7OH$. This body, chemically known as methyl-propyl phenol, occurs in several volatile oils, and is obtained by treating the residue left upon distilling the oils below 200° C. (392° F.) with solution of soda, whereby thymol is dissolved as sodium-thymol, $C_{10}H_{13}ONa$. When the solution has become clear by subsidence, thymol is liberated by means of hydrochloric acid and purified by distillation and crystallization; if necessary, it is also decolorized by treatment with animal charcoal.

Resins.

Comparatively little is known as yet regarding the chemical composition of resins which occur in plants either alone or in combination with volatile oils as oleoresins or with gums as gum resins. Investigations are now in progress in the hands of Prof. Tschirch of Berne, Switzerland, and his colaborers, and no doubt, in the course of a few years, much light will be shed upon this now rather obscure subject. This much has already been established, that resins are largely composed of organic acid esters or compound ethers of certain alcohols, to which latter the general name *resinol* has been applied; some of these alcohols give reactions similar to those characteristic of the tannins and have therefore been designated as *resinotannols*. Thus we have benzoresinol, storesinol, peruresinotannol, toluresinotannol, etc. Some resins have decidedly acid properties, while others are known to be anhydrides, as in the case of common pine resin or colophony, which is chiefly composed of abietic anhydride, $C_{44}H_{62}O_4$; one of the resins found in copaiba is a crystalline acid, called copaivic acid, having the elementary composition, $C_{20}H_{30}O_2$; the resin obtained from guaiacum wood and officially recognized as *guaiac*, consists largely (70 per cent. and over) of guaiaconic acid, $C_{19}H_{20}O_3$, to which the well-known color reactions of guaiac with oxidizing agents are due.

Resin of Scammony consists almost wholly of scammonin, $C_{34}H_{56}O_{16}$, the anhydride of scammonic acid, which behaves like a glucoside. *Jalap resin* consists of two distinct resins which can be separated from each other by ether, the one insoluble in that menstruum, and constituting about 70 per cent. of the official resin, consists almost entirely of convolvulin, $C_{31}H_{50}O_{16}$, an anhydride possessing glucosidal properties and being colorless when pure. The official *resin of podophyllum* is a complex mixture, containing an acid called podophyllinic acid, insoluble in ether, and a substance to which the name podophyllotoxin has been given; the latter, which constitutes about 50 per cent. of the official product, is said to be the active purgative principle. Both these substances are soluble in chloroform, and may be separated by addition of ether to the chloroformic solution, which precipitates podophyllinic acid; upon evaporation of the ethereal solution podophyllotoxin is obtained.

CHAPTER LVIII.

ORGANIC ACIDS.

Of the large number of compounds termed organic acids, only the few that are of special interest in pharmacy have been officially recognized. Organic acids are considered as derived from hydrocarbons or their alcohols, by replacement of hydrogen or hydroxyl by the univalent group carboxyl, CO_2H, and vary in their basicity as one, two, or three carboxyl groups may have been taken up, carrying with them one, two, or three atoms of replaceable hydrogen, as in the case of inorganic acids. The official organic acids are acetic acid, benzoic acid, citric acid, gallic acid, lactic acid, oleic acid, salicylic acid, stearic acid, tannic acid, and tartaric acid. Diluted hydrocyanic acid, although usually reckoned among the inorganic acids, is preferably considered at this point, since cyanogen is a carbon compound probably derived from hydrocarbons by substitution of nitrogen for hydrogen. Oxalic and valerianic acids, although not officially recognized, are both of interest to pharmacists, as is also meconic acid.

Acetic Acid, $HC_2H_3O_2$ or CH_3CO_2H. This acid has already been considered in connection with the derivatives of cellulose on page 549.

Benzoic Acid, $HC_7H_5O_2$ or $C_6H_5CO_2H$. Several methods are in use for obtaining this acid from benzoin, the balsamic resin from which it takes its name.

Both a dry and a wet process are employed for extracting the acid from the resin, in which it exists in a free state. The former is by sublimation, benzoin in coarse powder, which has been dried over lime, being heated in shallow iron pans covered with a porous diaphragm and connected with a suitable condenser, carefully regulated sand-bath heat being used so as to avoid contamination of the acid with other products, partly the result of decomposition, which volatilize at a temperature approaching 200° C. (392° F.). The yield of acid by this method ranges from 6 to 8 per cent. of the weight of benzoin used, the fused resin retaining a considerable portion which can be recovered by the wet method; sublimed acid is never chemically pure, being always accompanied by a volatile oil to which the peculiar odor of the acid is due.

The wet method consists in treating powdered benzoin for some time with warm milk of lime, and finally boiling the mixture and filtering while hot. The filtrate is supersaturated with hydrochloric

acid, the crude benzoic acid being allowed to crystallize and then purified by resolution in boiling water, with the addition of animal charcoal, filtered and again crystallized. In this process calcium benzoate, $Ca(C_7H_5O_2)_2$, is first formed and then decomposed with hydrochloric acid, whereby benzoic acid is liberated while calcium chloride remains in solution, thus, $Ca(C_7H_5O_2)_2 + 2HCl = 2HC_7H_5O_2 + CaCl_2$. Benzoic acid obtained by this method, is of fine white appearance, and devoid of the peculiar aroma of sublimed acid.

Of late years synthetic benzoic acid has been extensively produced, and the Pharmacopœia recognizes both the natural and synthetic products. The latter is made from toluene, $C_6H_5CH_3$, by passing chlorine gas into it while boiling until an increase in weight is no longer observed. Toluene is thereby converted into benzyl trichloride, $C_6H_5CCl_3$, which liquid, when treated with water under pressure, is converted into benzoic and hydrochloric acids, thus $C_6H_5CCl_3 + 2H_2O = C_6H_5CO_2H + 3HCl$; the benzoic acid is separated by straining and washed with cold water until free from hydrochloric acid. It is important in this process that the chlorine gas be passed into the boiling toluene in diffused daylight, to avoid the formation of other products.

Large quantities of benzoic acid are also made from the urine of cattle and horses, which contains hippuric acid, or benzoyl glycocoll. By boiling hippuric acid with strong hydrochloric acid, the former absorbs water and is split up into benzoic acid and glycocoll, thus: $C_6H_5COC_2H_3NHO_2 + H_2O = C_6H_5CO_2H + C_2H_3NH_2O_2$. Benzoic acid from this source is always accompanied by a fetid odor, which is removed by recrystallization and sublimation with benzoin.

Citric Acid, $H_3C_6H_5O_7 + H_2O$ or $C_3H_4OH(CO_2H)_3 + H_2O$. This acid belongs to the class known as fruit acids, and, although occurring in many plants, is obtained for use solely from lemons and limes. It is manufactured both in this country and Europe, on a large scale, from the juice of immature fruit, which contains from 6–8 per cent. of acid. The juice is first clarified by ebullition and then neutralized by addition of chalk, the resulting calcium citrate being washed with boiling water, in which it is sparingly soluble, and finally decomposed by means of diluted sulphuric acid; the newly formed calcium sulphate is removed by straining, the solution of citric acid being concentrated and allowed to crystallize in large wooden vats lined with lead. If necessary, the crystals of citric acid are redissolved in water, the solution being subsequently filtered through animal charcoal, to remove color, and recrystallized.

As citric acid crystallizes better from solutions containing a little sulphuric acid traces of the latter are generally found in the commercial article. Small particles of metal found adhering to the crystals and deposited in solutions thereof are lead, derived from the crystallizing vats. Contamination with crystals of tartaric acid can be readily detected by placing some of the crystals in a small dish

with a little solution of potassa; the crystals of citric acid slowly dissolve, while those of tartaric acid gradually become opaque, owing to the formation of acid potassium tartrate. The Pharmacopœia requires absolute purity for citric acid, with the exception of very small traces of sulphuric acid. The official test for the presence of tartaric and oxalic acids depends upon the solubility of potassium citrate in acetic acid, in which the tartrate and oxalate are insoluble.

Solutions of citric acid gradually separate fungous growths; this can, however, be prevented by addition of 5 or 10 per cent. of alcohol.

Diluted Hydrocyanic Acid. The official preparation of this name is an aqueous solution of gaseous hydrocyanic acid, HCN, prepared by decomposing a solution of potassium ferrocyanide with sulphuric acid, in a flask or retort, and conducting the resulting vapors into distilled water. In this process the following reactions occur: 1. The formation of hydroferrocyanic acid, thus, $K_4Fe(CN)_6 + 2H_2SO_4 = H_4Fe(CN)_6 + 2K_2SO_4$; 2. The decomposition of a further portion of potassium ferrocyanide by the newly formed acid in the presence of sulphuric acid, thus, $K_4Fe(CN)_6 + H_4Fe(CN)_6 + H_2SO_4 = 6HCN + K_2SO_4 + K_2Fe(Fe(CN)_6)$, hydrocyanic acid being evolved, while potassium sulphate and potassio-ferrous ferrocyanide, or Everitt's salt, remain in the flask or retort; the latter salt is white at first, but gradually changes to blue. Aqueous vapor of course passes over with the vapor of the acid, both of which are usually condensed in a Liebig condenser interposed between the retort and receiver. The directions of the Pharmacopœia are to continue distillation until the original volume of the mixture has been reduced to about one-half, and then to dilute the contents of the receiver with sufficient distilled water that the finished product shall contain 2 per cent. by weight of absolute hydrocyanic acid.

The quantity of water required for dilution of the distillate is readily ascertained by first determining volumetrically the amount of absolute HCN present; this is done by titrating a small weighed portion with decinormal silver nitrate solution, using potassium chromate as an indicator. Since silver chromate is soluble in both acid and alkaline liquids, it becomes necessary to neutralize the acid liquid, and for this purpose magnesium hydroxide is preferable to soda or potassa, as a slight excess of it is not hurtful—in fact, serves to sharpen the end reaction by providing a white background, against which the red color is more plainly seen. The equation, $HCN + AgNO_3 = AgCN + HNO_3$, shows that 26.98 parts of absolute hydrocyanic acid require 169.55 parts of silver nitrate for complete decomposition; hence each Cc. of $\frac{N}{10}$ $AgNO_3$ solution represents 0.002698 Gm. of HCN, and, as red silver chromate is not permanently formed until all hydrocyanic acid has been removed, the number of cubic centimeters of decinormal silver solution required to produce the permanent red color, multiplied by 0.002698,

gives the total quantity of hydrocyanic acid present in the sample used for the assay, which, multiplied by 100 and divided by the weight of the sample, expresses the percentage of absolute acid. Thus, if 0.27 Gm. of the distillate requires 3.4 Cc. of $\frac{2}{10}$ $AgNO_3$ solution, 3.4 per cent. of absolute HCN is present, for $3.4 \times 0.002698 = 0.0091732$, which multiplied by 100 and divided by 0.27 $= 3.39 +$ or 3.4. The amount of water necessary for dilution of the distillate can now be found by simple calculation, according to the rule stated on page 65, namely: multiply the total weight of the distillate by the percentage of absolute acid found and divide the product by the percentage required (which in this case is 2 per per cent.); the quotient indicates the weight to which the distillate must be brought by the addition of distilled water. If, from the weight so found, the weight of the original distillate be subtracted, the remainder will indicate the weight of water to be added.

As the vapor of hydrocyanic acid is very poisonous, special care must be observed that all joints of the flask, tubing, etc., be secure, so as to prevent leakage, and to guard against the bumping of the liquid in the flask, frequently observed, a tin hood may be placed over it or a spiral of glass or platinum be suspended in the liquid.

The alternative formula in the Pharmacopœia for making the official acid is simple, and offers a convenient method for rapidly preparing small quantities. Six Gm. of silver cyanide will yield 1.21+ Gm. of absolute hydrocyanic acid, which, dissolved in 60 Cc. of fluid as directed in the formula, makes a 2 per cent. solution; if strictly official hydrochloric acid be used, a very slight excess of the latter will be present.

Solutions of hydrocyanic acid are unstable, hence the official diluted acid is a very unsatisfactory preparation, even if carefully kept in small, tightly closed amber vials. Good sound corks are probably preferable to glass stoppers, as they fit more closely, as a rule. Various substances, such as sulphuric and hydrochloric acids, diluted alcohol, etc., have been suggested for the preservation of the diluted acid, but thus far none have proven strictly reliable.

A strong solution of hydrocyanic acid, known as Scheele's acid, contains 5 per cent. of absolute HCN, but is not used in this country for medicinal purposes.

The test with potassa, ferrous sulphate, and ferric chloride, mentioned in the Pharmacopœia, is generally known as Scheele's test for hydrocyanic acid, and depends upon the formation of ferric ferrocyanide, or Prussian blue, by alkali cyanides. The reactions occurring are as follows: 1. $HCN + KOH = KCN + H_2O$; 2. $18KCN + 3FeSO_4 + 2Fe_2Cl_6 = Fe_4(Fe(CN)_6)_3 + 12KCl + 3K_2SO_4$. In the presence of an excess of alkali hydroxide, however, as in the official test, the blue salt undergoes decomposition, alkali ferrocyanide entering into solution and ferroso-ferric hydroxide being precipitated; hence the addition of hydrochloric acid is made to redissolve the latter when ferric ferrocyanide will be precipitated.

GALLIC ACID, $HC_7H_5O_5 + H_2O$ or $C_6H_2(OH)_3CO_2H + H_2O$. When powdered nutgall is macerated for some time with water the astringent principle contained therein undergoes a change, becoming but sparingly soluble in cold water. Nutgalls contain tannin, which is now accepted to be an anhydride convertible into gallic acid by the absorption of water, thus: $C_{14}H_{10}O_9 + H_2O = 2HC_7H_5O_5$. The usual plan of obtaining gallic acid is to form a thin paste of nutgall with water, which is exposed to the air in a warm place for a month, with occasional stirring and replacement of water that may evaporate; at the end of that time the paste is expressed, the liquid being rejected, and the residue boiled with distilled water for a few minutes; the mixture is filtered while hot through animal charcoal and allowed to crystallize. The crystals, if not sufficiently free from color, are again dissolved in hot water, filtered as before, recrystallized, and dried.

The British Pharmacopœia directs to boil coarsely-powdered nutgall with diluted sulphuric acid for half an hour and strain the mixture while hot; upon cooling, the liquid separates crystals of gallic acid. The object of the sulphuric acid is simply to hasten the combination of the tannin with water, and thus save time.

Gallic acid is readily distinguished from tannic acid by its greatly decreased solubility in water, alcohol, and glycerin. Alkali citrates are said to increase the solubility of gallic acid in water to a marked degree. Its aqueous solution is, moreover, not precipitated by addition of albumin, starch, or gelatin solution, and the bluish-white precipitate formed upon addition of lime-water is redissolved by an excess of gallic acid; a large excess of lime-water causes the liquid to assume a pink tint. Gallic acid causes no precipitation in alkaloidal solutions.

Medicinally gallic acid is unlike tannic acid in so far that, externally applied, it exerts no astringent effect, although it readily controls passive hemorrhages when internally administered.

PYROGALLOL, also known as pyrogallic acid, is a derivative of gallic acid and recognized in the Pharmacopœia. Chemically it is a triatomic phenol, having the composition $C_6H_3(OH)_3$, and may be obtained by subliming previously dried gallic acid in an oil-bath at a temperature of 200° or 210° C. (392° or 410° F.); the yield by this method amounts to about 30 per cent. If gallic acid be heated with two or three times its weight of water for half an hour at the above-named temperature, under pressure in a suitable boiler, in such a manner that the liberated carbon dioxide can escape, a somewhat colored solution of pyrogallol will result, which, boiled with animal charcoal, filtered, and evaporated, yields an almost colorless crystalline mass, from which pure pyrogallol may be obtained; as the yield amounts to nearly 75 per cent. of the weight of gallic acid used, this process is preferred by manufacturers. In either case the chemical

change is the same, gallic acid being split up into pyrogallol and carbon dioxide, thus: $HC_7H_5O_5 = C_6H_3(OH)_3 + CO_2$.

Pyrogallol is readily darkened by exposure to air and light, owing to oxidation; hence it must be carefully preserved in tightly closed amber vials. It is very soluble in water, alcohol, and ether, and contamination with gallic acid may thus be detected.

As pyrogallol is poisonous, a derivative product has been introduced in its place, namely, *gallacetophenone*, or *gallactophenone*, prepared by heating a mixture of pyrogallol, zinc chloride, and glacial acetic acid to 148° C. (298.4° F.) and adding water to the fusion while hot; the resulting product may be recrystallized from boiling water. It occurs as a crystalline powder of dirty flesh-color, having the composition $C_6H_2(C_2H_3O)(OH)_3$.

Lactic Acid. The official acid is an aqueous solution of lactic acid, $HC_3H_5O_3$ or $CH_3CHOHCO_2H$, containing 75 per cent. by weight of the absolute acid. Three varieties of lactic acid are known, namely, isolactic or ethyledene lactic acid, sarcolactic acid, and ethylene lactic acid, of which the first alone is officially recognized; it is obtained by fermentation of a mixture of either milk-sugar or inverted sugar (see page 567), milk, or cheese and water, at a temperature between 25° and 35° C. (77° and 95° F.); chalk or zinc oxide is added to neutralize the acid as fast as formed, since butyric acid is otherwise apt to be produced if much free lactic acid is present. The resulting calcium, or zinc lactate, is subsequently recrystallized and decomposed by means of sulphuric acid or hydrogen sulphide, the mixture filtered and the solution of lactic acid evaporated. Complete evaporation of the water is not practicable, since the lactic acid would undergo decomposition, the elements of water being split off and insoluble lactic anhydride formed; hence the Pharmacopœia recognizes a very strong solution in place of the absolute acid. The temperature is an important factor in the fermentation of milk, as below 25° C. (77° F.) acetic acid will be formed, above 35° C. (95° F.) butyric acid; hence the largest yield of lactic acid is produced between these two degrees of heat.

Besides the official lactic acid two other varieties occur on the market, known as concentrated and dilute lactic acid respectively; but, since neither strength nor specific gravity is specified on the label, they should not be employed by pharmacists in prescriptions or otherwise.

The reaction between lactic acid, potassium permanganate, and sulphuric acid, mentioned in the Pharmacopœia, resulting in the development of an odor of aldehyde, has already been explained on page 477 under strontium lactate.

Meconic Acid, $H_3C_7HO_7 + 3H_2O$. This acid is of interest chiefly as a constituent of opium, and also on account of its peculiar reaction with ferric chloride, which can be used as a test for prepara-

tions of opium; ferric meconate possesses a blood-red color, like that of ferric acetate and sulphocyanate, but may be distinguished from the former by its indifference to dilute hydrochloric acid, and from the latter by its indifference to mercuric chloride. Reducing agents, such as stannous chloride and alkali hypochlorites, discharge the color of ferric meconate. Meconic acid may be obtained by precipitating a concentrated infusion of opium with calcium chloride, decomposing the resulting calcium meconate with warm dilute hydrochloric acid and recrystallizing from water.

Oleic Acid, $HC_{18}H_{33}O_2$ or $C_{17}H_{33}CO_2H$. In the chapter on fats and fixed oils this acid has been mentioned as being found in nearly all liquid fats. It is usually obtained of variable quality in a crude state in the manufacture of candles, being then known as *red oil;* for pharmaceutical purposes the crude acid can be sufficiently purified by simply cooling the same to 5° C. (41° F.) and separating the liquid portion from palmitic and other acids. Such an acid is recognized in the Pharmacopœia. A still purer acid may be obtained by saponifying expressed oil of almond with lead oxide, dissolving the lead oleate in petroleum benzin and decomposing the solution with dilute hydrochloric acid; after removal of the benzin by evaporation, the oleic acid may be washed with water. When perfectly pure, oleic acid is colorless, odorless, and tasteless, but rapidly becomes colored upon exposure to air and light.

The test for appreciable quantities of palmitic and stearic acids, mentioned in the Pharmacopœia, depends upon the formation of lead oleate, palmitate, and stearate, the former of which is soluble in ether, while the latter two are insoluble.

Oxalic Acid, $H_2C_2O_4 + 2H_2O$ or $(CO_2H)_2 + 2H_2O$. Although this acid occurs in numerous plants, chiefly in the form of acid potassium oxalate, it is obtained for the market wholly by synthetic methods. If sawdust be made into a pasty mass with strong solution of potassa, or potassa and soda, the mass then heated and kept at a temperature of 205° C. (401° F.) for one or two hours and dried, a gray powder of crude alkali oxalates will be obtained; by treatment with milk of lime, calcium oxalate results, which is then decomposed with sulphuric acid and the solution of oxalic acid is concentrated and crystallized. A much larger yield is said to be obtained by heating sodium hydroxide with carbonic oxide to 100° C. (212° F.), whereby sodium formate, $NaHCO_2$, is produced, which is then further heated to 400° C. (752° F.), with exclusion of air as far as possible, and converted into sodium oxalate, from which the acid is liberated as above.

Oxalic acid is used in medicine only in the form of ferrous and cerous oxalates, but is a valuable reagent in chemical analysis.

Salicylic Acid, $HC_7H_5O_3$ or $C_6H_4OHCO_2H$. Since the introduction of salicylic acid into medicine, nearly all thus used has been

prepared synthetically from carbolic acid or phenol; small quantities are also obtained by treating oil of wintergreen, methyl salicylate, with potassa and decomposing the resulting potassium salt with an acid. In the synthetic process, the first step is the manufacture of sodium carbolate, or sodium phenol, C_6H_5ONa, by saturating carbolic acid with sodium hydroxide. This compound is then dried and treated with carbon dioxide, whereby sodium phenol carbonate is formed, thus, $C_6H_5ONa + CO_2 = NaC_6H_5CO_3$; this is heated in tightly-closed vessels, or in retorts through which a stream of carbon dioxide is passing, to 130° C. (266° F.), when it is converted into sodium salicylate, $NaC_7H_5O_3$. This is the process now generally employed, and is a modification of Kolbe's original method, in which only one-half of the phenol was utilized, the remainder distilling over at a higher temperature. The crude sodium salicylate is dissolved in water and decomposed by means of hydrochloric acid; the resulting mixture is drained, washed with cold water, and finally dissolved in boiling water from which salicylic acid crystallizes on cooling and can be purified by solution in diluted alcohol, decolorized with animal charcoal, and recrystallized.

Salicylic acid furnishes several derivative products used in medicine, one of which is recognized in the Pharmacopœia under the name *Salol;* this can also be looked upon as a derivation of phenol; but, as it is more closely allied to salicylic acid in its therapeutic effects, it is generally classed with the same.

SALOL. This title is simply a copyrighted name applied to the phenyl ester of salicylic acid, more properly called *phenyl salicylate.* Several methods are known for preparing salol, such as treating a mixture of sodium phenol and sodium salicylate with phosphorus oxychloride, or passing a slow current of phosgene (carbonyl chloride) into a warm mixture of the two salts; in both cases new sodium salts are formed as by-products and the resulting salol is dissolved in alcohol and crystallized. A later and simpler process consists in heating salicylic acid, contained in a flask with a long narrow neck, in an oil-bath, to 220° or 230° C. (428° or 446° F.); air is excluded by passing a stream of carbon dioxide into the flask, the long neck of which permits only vapors of water and carbon dioxide to escape. The salicylic acid is first changed by heating into its anhydride, thus, $2HC_7H_5O_3 = (C_6H_4CO_2H)_2O + H_2O$; this is then split up into phenyl salicylate and carbon dioxide, thus: $(C_6H_4CO_2H)_2O = C_6H_5C_7H_5O_3 + CO_2$. The resulting compound is dissolved in alcohol and crystallized, as in the other methods.

Other derivatives of minor importance are: *salipyrine*, or antipyrine salicylate; *salophen*, a compound of salicylic acid and acetylamidophenol, a group far less poisonous than phenol; *saliphen*, a compound of salicylic acid and phenetidin; *salicylamide*, a compound produced by the action of ammonia on methyl salicylate; *diiodosalol*,

a condensation product of phenol and diiodosalicylic acid; *cresalol*, or cresol salicylate; *salumin*, aluminum salicylate.

STEARIC ACID, $HC_{18}H_{35}O_2$ or $C_{17}H_{35}CO_2H$. This acid, which is of very little use in pharmacy, except in the preparation of glycerin suppositories, is largely obtained in the manufacture of glycerin from tallow, by treatment with water and superheated steam, as explained on page 195. The commercial article is rarely pure, often consisting wholly of stearin; for pharmaceutical purposes, it should, at least, respond to the official requirement regarding the limit of undecomposed fat. Solubility in alcohol also serves to distinguish stearic acid from stearin.

TANNIC ACID, $HC_{14}H_9O_9$. The official tannic acid is that more specifically known as gallotannic acid, from its source, nut-gall, to distinguish it from related compounds found in the bark of various oaks, chestnut, etc.; it has, however, also been met in the leaves of tea and sumac. Absolutely pure gallotannic acid is no doubt digallic acid, or an anhydride of gallic acid, as stated on page 611, and, as such, its composition would be represented by the formula $(C_6H_2(OH)_2CO_2H)_2O$; the commercial article is, however, as a rule, contaminated with variable proportions of glucose in weak combination, which formerly gave support to the view that tannic acid was a glucoside. The true chemical character of tannin was first announced by Schiff, in 1871, and corroborated by Etti, in 1884. The subject of the various tannins has been carefully studied in this country, during the past five or six years, by Prof. H. R. Trimble, who has laid down the results of his labors in a valuable and extended monograph, entitled *The Tannins*, which work has been freely consulted by the writer.

Different methods are employed by manufacturers for the extraction of gallotannic acid, giving rise to the varieties known as ether-, alcohol-, and water-tannin. Chinese or Japanese galls are preferred to the Turkish variety, on account of their richness in tannic acid, from 60 to 65 per cent., and greater freedom from coloring matters. The ether method yields the best product. The finely cut galls are first exhausted with water, at a temperature of 40° or 60° C. (104° or 140° F.); the infusion is allowed to cool, then filtered and intimately mixed with commercial ether by agitation. When the emulsion has separated, the upper ethereal layer, containing coloring matter, resin, fat, gallic and ellagic acids, is removed and the aqueous fluid, after concentration, under reduced pressure, in a still, to a syrupy consistence, is spread, when cool, on tin plates, which are placed on a steam table and covered with a wooden box; this causes the tannin to puff up and dry and gives rise to the peculiar spongy character of commercial tannin. The so-called crystalline tannic acid of German manufacturers is obtained by introducing a very thick syrupy mass, prepared as above stated, into well tinned copper

vessels, with a perforated bottom, through which the mass slowly drops in long threads on to heated revolving cylinders, where it dries, and is removed in the form of thin needle-shaped particles.

Another plan is to extract the powdered nutgall with a mixture of ether four parts and alcohol one part, transferring the tannic acid to water by agitation with the latter, and then proceeding as before stated. This method is extensively employed.

Diluted alcohol is used in the preparation of alcohol-tannin by percolation, the tincture being concentrated and evaporated to dryness in a vacuum apparatus. Water-tannin is obtained by evaporating the aqueous infusion described above, to dryness, in a vacuum-pan. Neither of these products is as free from color or impurities as the first named or ether-tannin.

In 1893 Prof. Trimble suggested the use of acetone for the extraction of tannic acid from nutgall and exhibited, at Chicago, a sample of the acid, almost white, prepared by this method. The advantages claimed for this solvent are cheapness, thorough penetration, and rapidity of action.

Glucose, the most persistent impurity found in tannin, can be removed completely, as suggested by Trimble, by treatment with lead acetate and hydrogen sulphide and subsequent extraction of the tannin with acetic ether.

Gallotannic acid differs markedly from oak-bark tannins in its behavior toward several reagents, thus, while with lime water oak-tannins give a pink or red precipitate, gallotannic acid causes a blue precipitate; with bromine water gallotannic acid gives no precipitate, while oak-tannins cause a yellow precipitate; ferric chloride and ammonium hydroxide cause a green precipitate with oak tannins and a blue one with gallotannic acid, etc. The blue color sometimes observed in the case of oak-tannins with ferric salts is due to the presence of a foreign substance, pure oak-tannin showing only a green color. (Trimble.)

Owing to the ready discoloration of tannic acid by metallic iron in the presence of moisture, all contact with spatulas under such conditions must be avoided. Solutions of tannic acid change readily, particularly if exposed to air and light, gallic acid and probably *ellagic acid*, $C_{14}H_8O_9$, being gradually formed; such changes are retarded and even prevented by the presence of glycerin or alcohol in sufficient quantity.

The term tannin is now applied to the whole group of vegetable astringents, while the name tannic acid has been reserved for the particular product derived from nutgalls. The classification adopted by Trimble divides all tannins into two main groups, which may be distinguished from each other by the reactions above mentioned. All tannins should be soluble in water and precipitated by gelatin. The gallotannic-acid group includes, besides nutgall tannin, the tannins found in chestnut wood, chestnut bark, pomegranate bark, and sumac, while the oak-tannin group comprises the tannins from

different species of oak, from kino, catechu, krameria, tormentil, mangrove, and canaigre.

While, for technical purposes, the estimation of tannin in various tanning materials is often of importance, and is no doubt also valuable in chemical plant analysis, such determinations are not required in pharmacy. Advantage is taken of the well-known property of tannin to form insoluble compounds with gelatin (as demonstrated in the preparation of leather), and this operation is included in all methods of assay thus far published. A complete account of Löwenthal's method for estimating tannin, as modified by Von Schroeder, will be found in the *National Dispensatory*, 5th edit., p. 108.

TARTARIC ACID, $H_2C_4H_4O_6$ or $(CHOH)_2(CO_2H)_2$. This acid is even more widely distributed in the fruit of many plants than citric acid, occurring both in the free and combined state. For commercial purposes, it is obtained from crude or partially purified argols (see p. 432) by neutralizing the acid potassium tartrate in hot solution with chalk, whereby calcium and potassium tartrates are formed, and then decomposing the remaining potassium tartrate with calcium chloride; the resulting calcium tartrate is washed with water until tasteless and decomposed by digestion with sulphuric acid, when sparingly soluble calcium sulphate is formed and tartaric acid liberated, which latter enters into solution. After removal of the precipitated calcium sulphate by filtration, the solution of tartaric acid is concentrated and allowed to crystallize, the crystals, if necessary, being redissolved, digested with animal charcoal and recrystallized.

Tartaric acid is rarely found in the shops in other than powder form, and, as a rule, is free from impurities. The official test for oxalic and uvic acids, by means of calcium sulphate solution, depends upon the insolubility of calcium oxalate and uvate in the presence of ammonium salts, whereas calcium tartrate is but slowly deposited under like conditions; an excess of ammonia must be avoided, hence the Pharmacopœia directs incomplete neutralization. If crystallized tartaric acid is contaminated with uvic acid, the latter is readily detected by the milk-white appearance of its crystals, those of tartaric acid being translucent.

VALERIANIC ACID, $HC_5H_9O_2$ or $(CH_3)_2CH.CH_2.CO_2H$. As this acid occurs in a free state in valerian root, it may be obtained by distilling the root with water, neutralizing the aqueous portion of the distillate with soda, and decomposing this solution with sulphuric acid, it may then be purified by fractional distillation.

Commercially the acid is made by oxidation of amyl alcohol with a mixture of potassium dichromate and sulphuric acid, and neutralizing the distillate with sodium hydroxide; the resulting sodium valerianate is decomposed by means of sulphuric acid, when the liberated valerianic acid will rise as an oily layer. This is then freed from water by treatment with sulphuric acid, and carefully distilled.

The reaction taking place may be illustrated thus: $3C_5H_{11}OH + 2K_2Cr_2O_7 + 8H_2SO_4 = 3HC_5H_9O_2 + 2K_2SO_4 + 2Cr_2(SO_4)_3 + 11H_2O$. Since a small portion of the amyl alcohol escapes oxidation, it is attacked by the newly formed acid and passes over into the distillate as a compound ether, known as *amyl valerianate*, $C_5H_{11}C_5H_9O_2$; the name *apple oil* is given to this ether, on account of its apple-like odor when diluted. When the acid distillate is neutralized with soda the amyl valerianate separates as an oily liquid, and may be removed.

The solubility of valerianic acid in not less than 26, and not requiring over 30 times its weight of water, affords a ready means of discovering certain impurities; it should also produce a clear solution with a slight excess of ammonia water.

The only use made of valerianic acid in pharmacy is for the production of ammonium valerianate in the manufacture of the elixir of the same name.

CHAPTER LIX.

ALKALOIDS.

THE name alkaloids is applied to a large class of carbon compounds containing nitrogen, which are capable of neutralizing acids and forming salts. The basic properties of these compounds vary in intensity, some exhibiting but a feeble basic reaction, while others are capable of decomposing heavy metallic salts with the formation of metallic hydroxides. The term alkaloid was given to these so-called organic bases on account of their similarity in chemical character to alkalies, alkaloid meaning alkali-like.

Since the discovery of basic principles in both living and dead animal tissues the name alkaloids has generally been restricted to those nitrogenous bases derived from plants, the term *leucomaines* having been selected for the basic substances found in living animal tissues and *ptomaines* for those produced during putrefaction of dead animal tissues; the last named are still sometimes called cadaveric alkaloids. Chemists go even a step further by subdividing vegetable bases and reserving the name alkaloid for all those shown to be derived from pyridine, C_5H_5N, or quinoline, C_9H_7N, two simple bases found in coal tar.

The discovery of alkaloids occurred within the present century, in 1817, when Sertürner, a German apothecary, demonstrated the basic character of a substance obtained by him, in 1806, from opium, now known to us as morphine. In order to distinguish the basic from neutral vegetable principles a different terminology has been adopted for the two classes, which has been maintained in the Pharmacopœia and serves an excellent purpose. The ending *ine* (Latin *ina*) is applied to all basic plant products, while the ending *in* (Latin *inum*) is given to all neutral principles.

Alkaloids may be divided into two main classes as regards their constitution, namely, those containing carbon, hydrogen, nitrogen, and oxygen, and those containing only the first three elements; to the former, which are always solid, the name amides has been given, while the latter, which are liquid, are known as amines. Vegetable bases do not all possess the same saturating power for, while the majority are monacid in their character, several well-defined diacid bases are known. When brought together with acids they do not, like inorganic bases, cause the displacement of basylous hydrogen with the formation of water, but behave like ammonia, forming salts by simple addition. In regard to the naming of salts formed by the union of alkaloids with acids, it is customary in the case of oxygen

acids to follow the usual rule, thus: acetates, citrates, nitrates, phosphates, sulphates, etc., but, in the case of halogen acids, the proper name would seem to be obtained by changing the termination *ic* of the acid into *ide* for the salt, thus hydrobromide, hydrochloride, hydrocyanide, etc.; the Pharmacopœia has, however, adopted the plan of using the termination *ate* throughout, no matter what acid is in combination.

In a pure state alkaloids, with a few exceptions, are but sparingly soluble in cold water, but dissolve more or less readily in alcohol, chloroform, petroleum benzin, benzene, amyl alcohol, etc.; some, but not all, dissolve in ether. Salts of the alkaloids, as a rule, are soluble in water, but less so in other solvents.

In nature alkaloids rarely occur in a free state, being usually associated with an acid, which, in some instances, is a peculiar acid characteristic of the plant in which it is found, as igasuric acid in combination with the alkaloids of nux vomica, quinic acid of the cinchona barks, meconic acid in opium, etc.; many alkaloids occur in the plant as tannates. Alkaloids are not always restricted to special parts of the plant; while present to a much larger extent in some parts than in others, they are frequently met with in the root, stem, leaf, and fruit of the same plant. For their extraction various methods are employed: either the finely comminuted drug is exhausted with acidulated water, whereby the alkaloid is brought into solution as a new salt, which can then be decomposed and precipitated by means of an alkali and further purified by resolution in some appropriate solvent, filtration through animal charcoal and crystallization; or the drug may be exhausted with a neutral solvent, such as alcohol or diluted alcohol, the resulting tincture being acidulated, evaporated to remove fats, resins, etc., filtered, treated with water, and precipitated and purified as stated above. Advantage is taken of the difference in solubility between free alkaloids and their salts to separate and purify the product by the use of immiscible solvents, such as water and petroleum benzin, water and chloroform, water and ether, etc., whereby the alkaloid can be alternately transferred, in a combined or free state, from one fluid to another; this necessitates, of course, provision for bringing the liquids into intimate contact by agitators. This method, which is extensively employed in the assay of alkaloidal drugs, is termed by analysts the "shaking out process," because, on a small scale, the transfer is made in glass separators by rotation or shaking. In large operations, such as the manufacture of the cinchona alkaloids and others, kerosene or gasolene, closely allied to benzin, is now extensively employed on account of its solvent capacity, its cheapness, and ready separation from watery fluids. In the case of alkaloids which are volatile, the drug is placed in a still with some water, and, by the addition of a fixed alkali, the alkaloid is liberated, and with the aid of heat, passed over into a receiver containing acidulated water, when, having been obtained as an acid

salt, it can be further purified and isolated by one of the methods before mentioned.

To determine the presence of an alkaloid in any drug, the simplest plan is to macerate a small portion of the finely powdered article with about ten times its weight of Prollius' fluid, a liquid of remarkable penetrating power, composed of ether 325 Cc., alcohol 25 Cc., and stronger water of ammonia 10 Cc. The maceration should be conducted in a well-closed flask, for several hours, with frequent agitation, after which, some of the clear liquid is decanted into a glass separator (see Fig. 138) containing some 5 per cent. sulphuric acid, and, by means of careful but active rotation, any alkaloid present is transferred to the acid fluid; upon withdrawing this and warming on a water-bath to remove ether and alcohol, the addition of any of the general reagents mentioned below will produce a cloudiness or precipitate if alkaloids have been extracted.

Although particular alkaloids are only found in certain plants or species of plants, it often happens that several alkaloids are present in the same plant, ranging from 2 in nux vomica to 21 in opium and 32 in cinchona; rarely, however, does the number exceed 4. When pure, alkaloids are, as a rule, crystallizable, excepting the amines or liquid bases, without color, and have a definite melting-point, which latter is an important test of purity; their different solubilities have already been referred to. In solution, whether free or in a combined state, they are precipitated by a number of substances which are known as alkaloidal class reagents, and therefore incompatible with them in prescriptions. Such reagents are tannic acid, picric acid, mercuric chloride, and iodine with potassium iodide; besides these, the following tests for the presence of alkaloids are known by special names—*Mayer's reagent*, a solution of potassium mercuric iodide (see United States Pharmacopœia, page 486), *Marme's reagent*, a solution of potassium cadmium iodide, *Dragendorff's reagent*, a solution of potassium bismuth iodide, *Scheibler's reagent*, phosphotungstic acid, *Sonnenschein's reagent*, phosphomolybdic acid, and others. Many alkaloids give characteristic color reactions with acids and other reagents, by means of which their identity may be established; some of these reactions will be mentioned farther on in connection with the individual alkaloids. Very complete information regarding the behavior of alkaloids toward reagents as well as their source, solubilities, etc., is to be found in Sohn's *Dictionary of the Active Principles of Plants* (1894).

The quantitative determination of alkaloids in drugs may be effected both gravimetrically and volumetrically. The first method is largely employed, and is applicable whenever it is possible to isolate the alkaloid in the crystalline form or of any fair degree of purity, as in the official process for the morphiometric assay of opium or in determinations of cocaine. When, however, the alkaloidal residue is accompanied by appreciable quantities of impurities, such as coloring and resinous matters, the results obtained by

the gravimetric method are invariably too high and should be checked by volumetric estimation, which is best accomplished by solution of the residue in an excess of decinormal hydrochloric or sulphuric acid, with the aid of heat and titration of the excess of acid by means of centi- or decinormal alkali in the presence of a suitable indicator, as explained in the official process for the estimation of alkaloids in extract of nux vomica. In case but one alkaloid is present this method of titration leaves nothing whatever to desire, but when several alkaloids occur in a drug, lack of positive information as to the relative proportion in which these alkaloids are present causes a source of error which analysts thus far have not been able to overcome; in such cases, after careful purification of the alkaloidal residues by appropriate means, the gravimetric method is probably to be preferred for the determination of total alkaloids. The use of *Mayer's Solution* (decinormal solution of potassium mercuric iodide) was at one time advocated for the volumetric determination of alkaloids, on account of the formation of definite compounds between alkaloids and the double iodide; but since the results obtained have been found to vary with conditions not always controllable it has been abandoned, its use being now restricted to that of a qualitative reagent.

The Pharmacopœia gives specific directions for the determination of alkaloids in two drugs—cinchona and opium—and in eight galenical preparations—namely, the extract, fluid extract and tincture of nux vomica, and the extract, tincture, vinegar and wine of opium as well as the tincture of deodorized opium.

The official assay of cinchona involves the gravimetric determination of both total alkaloids and quinine; the former should reach not less than 5 per cent. of the weight of the drug, the latter at least 2.5 per cent. These percentages are now frequently exceeded in commercial cinchonas, barks containing 8 per cent. of total alkaloids and from 4 to 6 per cent. of quinine being not unusual; choice cinchona barks with 10 and 12 per cent. of quinine have even been found. The determination of the total alkaloids is readily understood; the ammonia present in the menstruum liberates the alkaloids, which are then taken up by the alcohol-chloroform mixture. Using definite proportions of drug and menstruum, an aliquot part of the filtrate represents a definite proportion of the drug. The residue of crude alkaloids is dissolved in diluted acid and again filtered to remove impurities, the filter being washed with acid water so as to recover any alkaloids retained in form of solution. The final addition of alkali again liberates the alkaloids, which are then taken up by repeated treatment with chloroform; the solution being evaporated and the residue dried to constant weight at 100° C. As 10 grammes of cinchona are represented in the chloroformic solution, the weight of residue multiplied by 10 must express the percentage of total alkaloid found. It frequently happens in the evaporation of chloroformic solutions of alkaloids that a varnish-like film is formed,

retaining traces of chloroform, hence it is advantageous to redissolve this film in a small quantity of ether which, upon being heated and evaporated, carries the last chloroform with it, thus insuring greater accuracy in weight.

The determination of quinine depends upon the greater solubility of this alkaloid in ether. By evaporating the original solution of alkaloids in the presence of powdered glass, the residue is obtained in a divided condition, in which it is readily acted upon by any solvent, hence, if treated with ether, this liquid will quickly dissolve any quinine present and as much of the other alkaloids as the quantity of ether used is capable of taking up. If now the residue be percolated with another like quantity of ether, the quinine having been taken up by the first treatment, a quantity of other alkaloids will again be dissolved corresponding to that dissolved by the first portion of ether and, by evaporation of this ether solution separately, the quantity so dissolved can be ascertained. Subtracting the weight of the second residue from the weight of residue obtained by evaporation of the first ether solution, the weight of the quinine dissolved is ascertained. Thus, if 5 Gm. of cinchona are represented in the alcohol-chloroform residue as officially indicated, and the residue from the first ethereal solution weighs 0.1875 Gm. and that from the second 0.0625 Gm., the difference, 0.125 Gm., indicates the weight of quinine present, which multiplied by 20 gives 2.5 as the percentage of quinine contained in the sample.

The morphiometric assay of opium directed in the Pharmacopœia is generally known as Squibb's method, having been first suggested by Dr. E. R. Squibb as a modification of Flückiger's method. Morphine, being present in opium chiefly as sulphate, is readily extracted with water, but, along with it, other substances, narcotine, codeine, coloring-matter, inorganic salts, etc., are also brought into solution, which it is proposed to remove entirely or retain in solution by the addition of alcohol and ether when the precipitation of the morphine is finally effected. As pure morphine is not entirely insoluble in water, a dilute mother-liquor is undesirable, hence concentration of the infusion is resorted to, in order to reduce the loss from this source; the addition of alcohol has been found advantageous in preventing the precipitation of coloring matter along with the morphine, and is by no means hurtful in the proportion directed. The ether removes narcotine and codeine, and, moreover, by its saturation of the aqueous fluid, still further reduces the solvent power of the latter on the freshly liberated morphine. The addition of ammonia water decomposes the morphine salt in solution and the free alkaloid gradually separates in the form of crystals. Morphine crystallizes with one molecule (5.94 per cent.) of water, and does not lose this water when dried at 60° C. (140° F.), hence, if accurate results are wanted, the crystals should be dried at that temperature, since the Pharmacopœia requires results in hydrated crystallized alkaloid. If the crystals are dried to constant weight, at 100° or 110° C. (212° or

230° F.), which is often more convenient than a regulated lower temperature, the weight of the anhydrous crystals should be multiplied by 1.063 to correspond to the hydrated crystals.

If the pharmacopœial directions be carefully observed, good results will almost invariably be secured. The highest percentages are generally obtained by allowing the crystals to separate during eighteen or twenty hours, but the longer the time the greater the impurities deposited along with the morphine. During the ordinary time allowed, from ten to twelve hours, these impurities are probably compensated for by the loss of morphine remaining in the mother-liquor, but, beyond this point, a correction often becomes necessary either by the lime-water test or ash test; pure morphine is soluble in 100 times its weight of official lime-water, hence, by treating 0.5 Gm. of morphine with 50 Cc. of lime-water, and ascertaining the weight of the insoluble residue when dry, the proportion of impurities present can readily be calculated.

The assay of extract of opium is very similarly conducted, and can be performed in less time, owing to the solubility of the extract in water. In the case of the tincture of opium it becomes necessary to get rid of the resinous and other matter taken up by the hydro-alcoholic menstruum; precipitation with water is therefore directed in the Pharmacopœia.

The official method of assay for extract of nux vomica is somewhat similar to that directed for cinchona. The first treatment with ammonia water and alcohol liberates the alkaloids and brings these into solution, whence they are abstracted by successive treatment with chloroform. The residue obtained by evaporation of the chloroformic solutions is dissolved in hot water, with the aid of a measured quantity of decinormal sulphuric acid, which converts the alkaloids into sulphates, an excess of acid remaining. After the addition of an indicator, centinormal alkali solution is added until the appearance of a permanent pinkish color indicates that a very slight excess of alkali is present. Centinormal alkali is used in preference to a decinormal solution to enable the operator to carefully neutralize the excess of acid without the danger of adding a marked excess of alkali. In order to bring the alkali solution to the value of the decinormal acid, it becomes necessary to divide the number of cubic centimeters of centinormal solution used by 10; subtracting the quotient so obtained from the number of cubic centimeters of decinormal acid first used gives the quantity of $\frac{N}{10}$ H_2SO_4 neutralized by the free alkaloids obtained from the extract. Since two alkaloids are known to be present in nux vomica, the neutralizing power of both must be taken into consideration in finding the factor indicating the value of 1 Cc. of decinormal acid. The proportions in which these alkaloids occur vary somewhat, but have been accepted as equal by analysts for the present, hence the Pharmacopœia directs that one-half the sum of their molecular weights shall be used, which divided by 10,000 yields ($334 + 394 = 728$; $728 \div 2 = 364$; $364 \div$

10,000 = 0.0364) 0.0364 as the amount of total alkaloids represented by 1 Cc. of $\frac{N}{10}$ H_2SO_4. As only 2 Gm. of extract are directed to be used for the assay, the percentage of alkaloids present may be found by multiplying either the number of cubic centimeters neutralized by the alkaloids by 1.82 (0.0364 × 50), or the number of cubic centimeters by 0.0364, and this product, which is the total amount of alkaloids in the two Gm., by 50.

The chemical constitution of absolutely pure alkaloids has been the subject of long and deep research. A French book published by Professor Pictet, of Geneva, Switzerland, in 1891, contains much valuable information along this line; a German translation by Wolffenstein is accessible to those familiar with the latter language. During the past four or five years Freund, of Germany, has added considerably to the knowledge of the constitution of alkaloids, and Wright, Dunstan, Ince, and Short, of England, have also contributed the results of their studies. Such investigations may eventually lead to the successful synthetic production of numerous natural alkaloids, as has already been possible in a few instances.

The following natural alkaloids are recognized in the Pharmacopœia in an uncombined state: *Atropine*, *Cinchonine*, *Codeine*, *Morphine*, *Quinine*, *Strychnine*, and *Veratrine*. *Caffeine*, although possessing but very feeble basic properties, must nevertheless also be placed in this class; by some authorities it is not considered an alkaloid at all, since it is not precipitated by potassium mercuric iodide solution and other class reagents.

Salts of the following natural alkaloids are officially recognized: Atropine, Cinchonidine, Cinchonine, Cocaine, Hyoscine, Hyoscyamine, Morphine, Pilocarpine, Physostigmine or Eserine, Quinine, Quinidine, Sparteine, and Strychnine; also salts of the following alkaloidal derivatives: Apomorphine, Hydrastinine.

The Official Alkaloids and Alkaloidal Salts.

APOMORPHINE HYDROCHLORIDE. $C_{17}H_{17}NO_2HCl$. Apomorphine may be classed among the so-called artificial alkaloids, being obtained by the action of hydrochloric acid on morphine or codeine. The process consists in heating either alkaloid with about 20 parts of pure hydrochloric acid in a sealed tube for several hours in an oil bath to between 140° and 150° C. (284° and 302° F.). After cooling the liquid contained in the tube is diluted with water, when, upon the addition of an excess of sodium bicarbonate, apomorphine will be precipitated; the mixture is filtered, and the new alkaloid extracted from the residue by means of ether or chloroform. The reaction occurring in the case of morphine appears to be simply an abstraction of the elements of water; thus, $C_{17}H_{19}NO_3 - H_2O = C_{17}H_{17}NO_2$; in the case of codeine, however, an intermediate product is formed, which is further split up into methyl chloride and apomorphine, thus, $C_{18}H_{21}NO_3 + HCl = C_{18}H_{20}ClNO_2 + H_2O$;

$C_{18}H_{20}ClNO_2 = C_{17}H_{17}NO_2 + CH_3Cl$. If a few drops of hydrochloric acid be added to the ethereal or chloroformic solution above mentioned, apomorphine hydrochloride will separate in a crystalline form, and may be recrystallized from boiling water. The salt must be thoroughly dried over sulphuric acid and carefully protected against moisture, air, and light, otherwise it soon assumes a green color, due to oxidation.

Apomorphine hydrochloride is always dispensed in the form of aqueous solutions, and amber vials should be used for the same; the gradual green coloration of the solution can be prevented by addition of a few drops of hydrochloric or acetic acid. A solution of this salt may be readily distinguished from one of morphine hydrochloride by precipitating the alkaloid with sodium bicarbonate; the amorphous residue, in the case of apomorphine, soon turns green, and imparts to its solution in ether a purplish-violet color, and to a chloroformic solution a blue color. The alkaloid morphine is insoluble in these liquids.

ATROPINE. $C_{17}H_{23}NO_3$. This alkaloid belongs to the class known as mydriatic alkaloids, so named on account of their property of causing dilatation of the pupil of the eye, which occur in belladonna, duboisia, hyoscyamus, scopolia, and stramonium, and include atropine, belladonnine, hyoscine, and hyoscyamine; daturine and duboisine, formerly considered as distinct alkaloids, are now known to be identical with atropine and hyoscyamine respectively. Atropine, hyoscine, and hyoscyamine have the same percentage composition, and the last named can be converted into the first by the action of alkalies in alcoholic solution. All three alkaloids are easily decomposed by strong acids and alkalies.

Atropine is found chiefly in belladonna, being obtained preferably from the root, as the latter is richer in alkaloid and free from chlorophyll. The finely powdered root is exhausted with alcohol, and the percolate mixed with calcium hydroxide to decompose the natural salt of atropine and liberate the alkaloid, which remains in solution; after filtration, the filtrate is acidulated with diluted sulphuric acid, concentrated to remove alcohol, fat, and resin, and treated with alkali carbonate in excess. The precipitated atropine is removed, washed with water, and dissolved in alcohol; to this alcoholic solution water is added, drop by drop, to incipient turbidity, and the alkaloid allowed to crystallize. Other bases present remain in the mother-liquor, but small quantities of hyoscyamine always accompany the commercial article.

Atropine is a monacid base possessing marked alkaline properties; it is capable of decomposing mercuric and mercurous chloride with the formation of the respective oxides; it also reddens phenolphtalein paper, and restores the blue color of reddened litmus.

The melting-point of atropine is incorrectly stated in the Pharmacopœia to be 108° C. (226.4° F.); if pure, it melts at 115° C.

(239° F.), but this is largely affected by the presence of hyoscyamine, which itself melts at 108° C.

ATROPINE SULPHATE. $(C_{17}H_{23}NO_3)_2\ H_2SO_4$. This salt may be prepared either by adding atropine slowly to a mixture of sulphuric acid and alcohol or by dissolving atropine mixed with water by means of diluted sulphuric acid. In either case a perfectly neutral solution must be obtained, which is then evaporated to dryness, at a temperature below 40° C. (104° F.). Some of the commercial salts show an acid reaction when dissolved in water, and are, therefore, unfit for use.

CAFFEINE. $C_8H_{10}N_4O_2 + H_2O$. This feebly basic substance occurs in a number of plants belonging to different natural orders, thus, in coffee, tea, kola, and paullinia, associated with tannin and varies in amount from less than 1 to 5 per cent. of the dried material. For commercial purposes it is usually obtained from powdered coffee-beans, not roasted, or preferably the fine unsalable particles of tea-leaves (tea-leaves being also much richer in caffeine), by exhausting the same with hot water, adding a solution of lead acetate in slight excess, whereby tannin and coloring-matters are precipitated, filtering, adding ammonia water to remove excess of lead salt and again filtering. The filtrate is concentrated, hydrogen sulphide added to remove any lead still remaining, filtered and further evaporated to the crystallizing-point. Milk of lime is also sometimes used to remove tannin, fat, coloring-matter, etc., and is added to the powdered material, the mixture being then exhausted with warm 80 per cent. alcohol; the percolate is diluted with about one-sixth its volume of water and distilled to recover the alcohol. The aqueous residue is filtered and crystallized. If necessary, the product is redissolved, filtered through bone-black, and again crystallized.

Caffeine is very soluble in boiling water, 2 parts, and also in chloroform, 7 parts, but requires 80 parts of cold water for solution, which quantity is very materially reduced, however, by the presence of certain other substances, such as sodium benzoate, bromide, salicylate, and cinnamate, and even antipyrine.

The caffeine derived from different sources is now considered identical, although the names theine and guaranine are still occasionally used.

Chemically, caffeine is a derivative of xanthine, as shown by the murexide reaction mentioned below, being known as trimethyl xanthine, $C_5H(CH_3)_3N_4O_2$, and sometimes also called methyl theobromine. It has been prepared synthetically by the action of methyl iodide on theobromine, $C_5H(CH_3)_2N_4O_2$, a basic substance found in cacao beans.

When treated with chlorine water or hydrochloric acid and potassium chlorate, as directed in the Pharmacopœia, caffeine yields, upon evaporation to dryness, a substance known as *amalic acid*, which, in

the presence of air and ammonia, forms murexoin or tetramethyl murexide, $C_8(CH_3)_4N_5O_6(NH_4)$, of a rich purple color; this test is characteristic of caffeine and theobromine.

CINCHONIDINE SULPHATE. $(C_{19}H_{22}N_2O)_2H_2SO_4 + 3H_2O$. Cinchonidine is one of the four important alkaloids found, among a large number (32), in cinchona bark and occurs in greater proportion in the so-called red bark, derived from cinchona succirubra, than in others. The sulphate is obtained from the mother-liquors left in the manufacture of quinine sulphate and is purified by fractional crystallization. The official salt, containing but three molecules, 7.29 + per cent., of water of crystallization, is the result of using a hot concentrated solution, for, if the salt be crystallized from weaker solutions it will contain six molecules, or 14.6 per cent. of water.

Absolute purity of the salt is not practicable, nor demanded by the Pharmacopœia, hence a slight fluorescence is sometimes observed in solutions of the salt made with diluted sulphuric acid. The official test with Rochelle salt and ammonia water depends upon the insolubility of cinchonidine tartrate, the tartrates of cinchonine and quinidine being dissolved and reprecipitated upon addition of ammonia.

CINCHONINE. $C_{19}H_{22}N_2O$. This base is present in all cinchona barks and may be obtained from the mother-liquors of quinine sulphate, by precipitating these, after dilution, with ammonia or soda, and dissolving the resulting precipitate in boiling alcohol, when upon cooling cinchonine will separate in a crystalline form, being far less soluble in cold alcohol than the other alkaloids present. If boiling alcohol be used for the extraction of the mixed bases in the manufacture of quinine sulphate, cinchonine will also crystallize from this upon cooling. In either case the alkaloid may be purified by resolution and recrystallization.

Pure cinchonine, like pure cinchonidine, shows no blue fluorescence in a solution made with sulphuric acid, nor is either alkaloid appreciably soluble in ether. They differ from each other in their optical rotation, cinchonine being dextrorotatory and cinchonidine laevorotatory.

CINCHONINE SULPHATE. $(C_{19}H_{22}N_2O)_2H_2SO_4 + 2H_2O$. The usual process for making this salt is to dissolve the alkaloid cinchonine in warm diluted sulphuric acid until the acid is neutralized and then concentrate and crystallize the solution. The Pharmacopœia requires the absence of more than 5 per cent. of water of crystallization. Cinchonine sulphate may be readily distinguished from cinchonidine sulphate by its greater solubility in chloroform, requiring not over 80 parts for solution, while the latter requires about 1320 parts.

COCAINE HYDROCHLORIDE. $C_{17}H_{21}NO_4.HCl$. The leaves of erythroxylon coca contain a number of basic principles, all derivatives of ecgonine, $C_9H_{15}NO_3$, of which cocaine is the most important; other non-crystallizable bases are truxilline or isatropylcocaine (known also as cocamine), $C_{19}H_{23}NO_4$, hygrine, $C_{12}H_{13}N$, and cinnamylcocaine, $C_{19}H_{23}NO_4$. Cocaine appears in the plant united with cocatannic acid. The processes employed for the isolation of cocaine are usually guarded as secrets by manufacturers, and it is known that large quantities of the alkaloid are now prepared synthetically, owing to the difficulty of extracting *pure* cocaine in remunerative quantities from the drug.

When finely powdered coca leaves are moistened with solution of sodium hydroxide and then treated with petroleum ether, kerosene, or gasolene, the alkaloids present are liberated and taken up by the menstruum, from which they can be transferred, as salts, to diluted sulphuric acid, through intimate contact by agitation. If to this acid solution solution of soda be added in excess, cocaine mixed with some of the lesser alkaloids will be precipitated, the bulk of the hygrine, however, remaining in solution; the crude cocaine may be removed by filtration and expression and purified by crystallization from alcohol. As the yield of cocaine is known to decrease materially by transportation, no doubt owing to decomposition, the result of fermentation in the imperfectly dried and tightly packed leaves, the bulk of the natural alkaloid is now manufactured in South America, in places adjacent to the source of gathering the leaves, processes of extraction very similar to the above being employed.

In order to avoid loss of the decomposition-products and other alkaloids accompanying cocaine in the crude article, the pure alkaloid is now extensively prepared by synthesis, in the following manner, which is possible, since the chemical constitution of cocaine is definitely known to be methyl benzoyl ecgonine. Boiling the mixed bases with hydrochloric acid converts them all into ecgonine, $C_9H_{15}NO_3$, and if ecgonine hydrochloride, $C_9H_{15}NO_3HCl$, be dissolved in methyl alcohol and the solution treated with dry hydrochloric acid gas, hydrochloride of methyl ecgonine, $C_9H_{14}CH_3NO_3HCl$, will be formed and can be crystallized from an alcoholic solution. By heating this latter compound with benzoyl chloride, C_7H_5OCl, in a water-bath, until hydrochloric acid is no longer evolved and a homogeneous mass results, cocaine is obtained, which is freed from benzoic acid by solution in water, filtration, precipitation of the alkaloid with ammonia and recrystallization from alcohol. Synthetic cocaine is identical in every respect with the natural alkaloid.

Cocaine hydrochloride is prepared by dissolving the pure alkaloid in alcoholic solution of hydrochloric acid and crystallizing the anhydrous salt, which latter only is recognized in the Pharmacopœia.

The two most important tests for the purity of the salt are those with potassium permanganate and with hot hydrochloric acid; the former, given in the Pharmacopœia, depends upon the stability of

cocaine permanganate. If pure cocaine hydrochloride be carefully warmed in a test-tube with about four times its weight of strong hydrochloric acid, until the mixture begins to boil, a colorless solution results; the degree of color, if there be any, is, in a measure, an indication of the amount of impurities present; the color thus obtained should never exceed that of a pale wine tint.

CODEINE. $C_{18}H_{21}NO_3 + H_2O$. This alkaloid is obtained from opium, where it exists to the extent of from $\frac{1}{3}$ to $\frac{3}{4}$ per cent. along with morphine, by treatment of an aqueous infusion of opium with chalk and calcium chloride, whereby codeine and morphine hydrochlorides are formed and can be purified by repeated crystallization. If a solution of these crystals be treated with ammonia, morphine will be precipitated while codeine remains in solution and may be recovered by crystallization; if potassa or soda be used in place of ammonia, codeine will be precipitated, the morphine remaining in solution.

Codeine crystallizes from an aqueous solution with one molecule (5.67 per cent.) of water, which constitutes the official article; if crystallized from ether or carbon disulphide, it is anhydrous. Its crystals are larger and more soluble in water than those of any other alkaloid. Although the free alkaloid only is recognized in the Pharmacopœia, the sulphate and phosphate of codeine are largely used by physicians; they can be prepared by neutralizing an aqueous solution of the alkaloid with the respective acid and crystallizing.

Chemically, codeine is closely allied to morphine, as shown by the formula, $C_{17}H_{18}CH_3NO_3$, which differs from that of morphine by a methyl group, hence the name methyl morphine. When heated with strong hydrochloric acid, in a sealed tube, both alkaloids yield apomorphine, but, if heated to 180° C. (356° F.) with a concentrated solution of zinc chloride, codeine yields *apocodeine*, whilst morphine again yields apomorphine. Codeine has been prepared synthetically by heating morphine with methyl iodide. The name codeine is derived from the Greek word *κώδεια*, meaning head, referring to the source of the alkaloid, poppy heads.

HYDRASTININE HYDROCHLORIDE. $C_{11}H_{11}NO_2HCl$. The alkaloid hydrastinine does not occur in any plant, but is an artificial base obtained by oxidation of hydrastine—the white alkaloid found in hydrastis—in acid solution, by means of potassium dichromate or permanganate. Since the use of this basic principle and its salts is very limited, it seems particularly strange that the Pharmacopœia should have failed to recognize hydrastine, which is far more extensively employed, and yet have given prominence to one of its derivative products.

This salt differs from hydrastine hydrochloride in being colored; its aqueous solution is not affected by ammonia water, while hydrastine is precipitated from a solution of its salts under like circumstances.

HYOSCINE HYDROBROMIDE. $C_{17}H_{21}NO_4HBr+3H_2O$, or $C_{17}H_{23}NO_3HBr+3H_2O$. Hyoscine is an amorphous alkaloid, occurring in the plants belonging to the natural order of the Solanaceæ, associated with hyoscyamine and atropine. It is found in largest quantity, about $\frac{1}{50}$ or $\frac{1}{30}$ per cent., in the seed of hyoscyamus and the leaves of the duboisia. For commercial purposes hyoscine is obtained from either of the above sources, chiefly henbane seed, by exhausting the drug with 80 per cent. alcohol, recovering the alcohol by distillation and setting the residue aside for several days, when a fatty layer separates from the aqueous solution of the mixed bases in combination with organic acids. By addition of alkali carbonate to the aqueous solution, the alkaloids are liberated and may be abstracted by agitation with ether. Upon evaporation of the ether a syrupy liquid is obtained, from which nearly all the hyoscyamine present crystallizes out; the hyoscine may be isolated from the mother-liquor by converting it into an aurochloride, separating the same by fractional crystallization, redissolving in water, and, after removal of the gold by means of hydrogen sulphide, precipitating the hyoscine from the filtrate, by alkali carbonate, in the form of an oily layer, which may be purified by solution in chloroform and evaporation of the solvent. When perfectly pure, hyoscine occurs as a tenacious syrupy mass. No doubt manufacturers employ a less expensive method of separating hyoscine from hyoscyamine, but guard it as a secret.

The official salt may be obtained by dissolving hyoscine in a very slight excess of diluted hydrobromic acid, concentrating the solution and allowing it to crystallize. It contains about 12.5 per cent. of water.

Although the Pharmacopœia has adopted for hyoscine the formula of Hesse and Schmidt, $C_{17}H_{21}NO_4$, Ladenburg and other authorities give it as $C_{17}H_{23}NO_3$, making the alkaloid isomeric with atropine and hyoscyamine.

HYOSCYAMINE HYDROBROMIDE. $C_{17}H_{23}NO_3HBr$. The method for obtaining the alkaloid hyoscyamine has been outlined in the preceding article. The hydrobromide may be prepared like the corresponding salt of hyoscine, but forms anhydrous crystals.

HYOSCYAMINE SULPHATE. $(C_{17}H_{23}NO_3)_2H_2SO_4$. This salt is obtained by dissolving hyoscyamine in sufficient diluted sulphuric acid to form a neutral solution, which, after proper concentration, is allowed to crystallize. Both this and the preceding salt may be distinguished from the corresponding salts of atropine by forming, upon addition of gold chloride test-solution and recrystallization of the precipitate from boiling-water, minute, lustrous, golden-yellow scales, while the atropine salts yield crystals forming a yellow, lustreless powder, on drying.

MORPHINE. $C_{17}H_{19}NO_3+H_2O$. This is the most important of the large number of alkaloids found in opium, and, as before stated,

was the first basic principle isolated from plants. It was called by its discoverer *morphium*, after the Greek deity *Μορφεύς*, the God of sleep, on account of its sleep-producing properties.

Morphine is present in opium in varying quantities, reaching as high as 12 or 14 per cent. in some samples of commercial opium not dried; the Pharmacopœia recognizes no undried opium containing less than 9 per cent. of morphine and demands from 13 to 15 per cent. in the powdered article. It was formerly supposed to exist in combination with meconic acid only, but is now known to be present largely, if not altogether, as sulphate.

Morphine for commerce may be obtained in several ways; the natural salts being soluble in cold water, opium is exhausted with this menstruum, and the infusion, after concentration, treated either with sodium carbonate or with chalk and calcium chloride; the latter process is preferable, since meconic acid and coloring-matters are precipitated as lime compounds, while the alkaloids are converted into soluble chlorides. After filtration the filtrate is concentrated, and yields a crystalline mass of morphine and codeine chlorides; narcotine remains in solution in the dark-colored mother-liquors; the crystals are purified by resolution in water, filtration through animal charcoal, and recrystallization. Finally, the mixed salts are dissolved in water and decomposed by addition of ammonia water, whereby the morphine is precipitated, the codeine remaining in solution. The morphine is subsequently recrystallized from hot alcohol. Other methods are known, and manufacturers, probably in each case, follow some favorite process.

The alkaloid morphine is rarely used in pharmacy, except in the preparation of the various oleates of morphine. The official article contains about 5.94 per cent. of water of crystallization, which it readily loses at 110° C. (230° F.), but parts with very slowly at the temperature of a boiling-water bath. Owing to the solubility of morphine in solutions of the fixed alkali hydroxides and insolubility in ether, as well as its characteristic reactions with oxidizing agents, it is readily distinguished from other alkaloids.

Morphine Acetate. $C_{17}H_{19}NO_3C_2H_3O_2+3H_2O$. This salt is prepared by dissolving the alkaloid morphine in a slight excess of diluted acetic acid and evaporating the solution to dryness with the aid of a moderate heat, so as to avoid decomposition. It never occurs in a crystalline form on the market, but always in powder form. Morphine acetate is easily decomposed by heat or exposure to air, and the partial insolubility of the salt sometimes observed is due to such change, caused either by carelessness during evaporation of the solution or exposure to air and light; when such a condition exists a drop or two of diluted acetic acid should be added to produce perfect solution. This salt is preferred by German practitioners of medicine, while in Great Britain the hydrochloride is given the

preference, and in this country the sulphate; of the three salts, the acetate is the most soluble in water.

MORPHINE HYDROCHLORIDE. $C_{17}H_{19}NO_3HCl + 3H_2O$. By using dilute hydrochloric acid as a solvent for morphine alkaloid a solution of this salt is obtained, which, upon concentration, yields well-defined crystals containing 14.38 per cent. of water; an excess of acid should be avoided, as the salt is very stable and must have a neutral reaction. As made in this country, morphine hydrochloride occurs in large masses of feathery crystals, and is more bulky, weight for weight, than the sulphate. It can be rendered perfectly anhydrous at a temperature of 100° C. (212° F.).

MORPHINE SULPHATE. $(C_{17}H_{19}NO_3)_2H_2SO_4 + 5H_2O$. Next to quinine sulphate there is probably no alkaloidal salt more extensively used by physicians than this one, and, unfortunately, its unauthorized use among the laity is on the increase in this country, owing to the lack of sufficient legal restrictions and the cupidity of certain pharmacists and dealers in drugs. Like the two preceding salts, morphine sulphate is made from the alkaloid by dissolving the same in sufficient diluted sulphuric acid to form a neutral solution and setting this aside to crystallize. The official salt contains 11.87 per cent. of water of crystallization, of which, however, only a part, 7.12 per cent., can be expelled at the temperature of a boiling-water bath.

An aqueous solution of morphine sulphate is largely used in some parts of this country under the name *Magendie's Solution;* it contains 16 grains of the salt in each fluidounce, which is equal to about $\frac{1}{30}$ of a grain in each minim. As aqueous solutions of morphine sulphate do not keep well for any length of time, one-half grain of salicylic acid has been used in each fluidounce of this solution with excellent results. Prior to 1880, a solution of morphine sulphate was officially recognized in the Pharmacopœia; this solution contained only one grain of the salt in each fluidounce, and must not be confounded with Magendie's solution.

PHYSOSTIGMINE SALICYLATE. $C_{15}H_{21}N_3O_2C_7H_6O_3$. The alkaloid physostigmine occurs in calabar beans to the extent of rarely more than one-tenth of one per cent., and its isolation requires considerable care, owing to its ready decomposition. The usual method of extraction is to exhaust the powdered bean with 85 per cent. alcohol, and concentrate the tincture in a vacuum apparatus to a syrupy consistence; the resulting extract separates into an upper layer, consisting of fat, etc., and a lower, aqueous solution of the natural salts of the alkaloids. By treating the aqueous layer with sodium bicarbonate, and then repeatedly shaking with ether, the liberated physostigmine may be extracted; the ethereal solution is next treated with diluted sulphuric acid, so as to obtain a solution of the alkaloid as sulphate, leaving impurities, fat, resin, etc., in the ethereal liquid.

The pure alkaloid is finally obtained by decomposing the sulphate with sodium bicarbonate, extracting again with ether and crystallizing. Heat must be avoided as far as possible, also the use of strong alkalies, as in the case of the mydriatic and other easily decomposable alkaloids.

The name *eserine*, by which physostigmine is also known, was derived from the word *esère*, meaning split nut, the name applied by the African negroes to the calabar bean. Calaberine is the name given to another alkaloid present in the bean, which, however, is insoluble in ether.

Physostigmine salicylate may be prepared by neutralizing a solution of the alkaloid in absolute alcohol with pure salicylic acid; the salt gradually separates in needle-shaped crystals, free from color, which can be then drained and dried.

Some of the salts of physostigmine and their aqueous solutions readily assume a reddish color when exposed to light and air, hence they must be dispensed in tightly closed amber vials; the name rubereserine has been given to the red substance thus formed. The salicylate is less liable to change by exposure to light than the other salts; but, owing to its slight solubility in water, is far less used than the sulphate.

PHYSOSTIGMINE SULPHATE. $(C_{15}H_{21}N_3O_2)_2H_2SO_4$. The preparation of this salt has already been indicated above in connection with the extraction of the alkaloid from the drug; by carefully neutralizing an alcoholic solution of physostigmine with sulphuric acid and concentrating the solution to a syrupy liquid, at moderate temperature, crystals of the salt may be obtained. The commercial article is rarely entirely free from color, generally occurring in yellowish, amorphous, very hygroscopic masses.

This and the preceding salt are used, in the form of solution and gelatin disks, for the purpose of producing myosis or contraction of the pupil of the eye.

PILOCARPINE HYDROCHLORIDE. $C_{11}H_{16}N_2O_2HCl$. Pilocarpus or jaborandi leaves contain three alkaloids, of which only one, however, is of pharmaceutical interest—namely, pilocarpine, which occurs in variable quantities, often not exceeding one-half per cent. It may be extracted by means of alcohol acidulated with hydrochloric acid; the resulting tincture is concentrated, when resin, fat, etc., separate, the remaining liquid is treated with ammonia water and the liberated alkaloids extracted by repeated agitation with chloroform, the chloroformic solution being evaporated to a syrupy consistence and neutralized with nitric acid, the resulting nitrates being taken up with alcohol, from which the pilocarpine nitrate crystallizes while the nitrates of pilocarpidine and jaborine remain in solution; by dissolving the crystals in water, adding ammonia water in excess and shaking the mixture with chloroform, pure pilo-

carpine may be obtained as a colorless syrupy liquid upon evaporation of the chloroform solution.

The hydrochloride is prepared by neutralizing the alkaloid with dilute hydrochloric acid and evaporating the resulting solution to dryness, when it is obtained as a crystalline powder.

The salts of pilocarpine are used chiefly as diaphoretics and sialagogues, but possess also decided myotic properties, like physostigmine.

QUINIDINE SULPHATE. $(C_{20}H_{24}N_2O_2)_2H_2SO_4+2H_2O$. Quinidine usually remains in the mother-liquors from the crystallization of quinine sulphate, from which it may be obtained by adding a large excess of ammonia water, whereby cinchonine and cinchonidine are thrown down, while quinidine remains in solution; it can subsequently be precipitated by means of caustic soda and dissolved in diluted sulphuric acid, the resulting salt being purified by recrystallization. From the purified alkaloid, obtained by precipitation with soda, the sulphate can be readily prepared by solution in just sufficient warm diluted acid to neutralize the same, and crystallizing; if an excess of acid be used, a salt differing from the official salt will be formed.

Quinidine sulphate somewhat resembles official quinine sulphate in appearance, and has some chemical properties in common with it, but may be distinguished by its greater solubility in water and in alcohol and by being precipitated in concentrated aqueous solution by potassium iodide. Its solutions, like those of quinine sulphate, form thalleioquin and show a blue fluorescence when acidulated with sulphuric acid.

QUININE. $C_{20}H_{24}N_2O_2+3H_2O$. This is, no doubt, the most important and extensively used of all alkaloids. It occurs to a varying extent in the different species of cinchona, the yield having increased greatly with careful cultivation of the trees in India, Java, etc. The bases present in cinchona bark exist in combination with quinic or kinic, quinovic, and cinchotannic acids, and are usually extracted by means of acidulated water. The infusion is concentrated and mixed with milk of lime, whereby the alkaloids are liberated while the calcium compounds of the organic acids are precipitated together with much coloring-matter. By straining the mixture and exhausting the residue repeatedly with boiling alcohol, amyl alcohol, petroleum benzin or kerosene, a solution of the crude alkaloids is obtained, from which the latter may be transferred as sulphates by treatment with dilute sulphuric acid. Another plan is to mix the powdered bark with solution of soda or milk of lime, whereby the natural combinations are broken up and the alkaloids liberated; the mixture is then exhausted, in a suitable apparatus, with hot alcohol or kerosene, from which, after proper concentration, the alkaloids are extracted as acid sulphates by means of sulpuhric acid.

In either case the acid solution is treated with animal charcoal, and the liquid, while hot, after filtration, neutralized with solution of soda, when, upon cooling, neutral quinine sulphate crystallizes out and may be purified by resolution, recrystallization, etc. The other alkaloids, including also small quantities of quinine sulphate, remain in the mother-liquor and may be recovered as stated elsewhere.

From the purified quinine sulphate the alkaloid may be obtained by precipitation with soda, after solution of the salt in water with the aid of an acid.

Official quinine alkaloid contains about 14.3 per cent. of water of crystallization and melts at a comparatively low temperature, 57° C. (134.6° F.); at 100° C. (212° F.), about two-thirds of the water is expelled, but it does not become anhydrous until a temperature of 125° C. (257° F.) is reached. The commercial article varies considerably in appearance and solubility, due, no doubt, to different methods of manufacture; some is crumbly, compact, and idioelectric, dissolving slowly in alcohol and even dilute acids, while another lot is light, possesses no electric tendency, and dissolves readily.

The test for appreciable quantities of other cinchona alkaloids depends upon the greater solubility of quinine alkaloid in ammonia water, 0.5 Gm. of the freshly precipitated alkaloid being soluble in 7 Cc. of 10 per cent. ammonia water at 15° C. (59° F.). The increased quantity of ammonia water allowed by the Pharmacopœia in case the maceration of the quinine sulphate with water has been made at a temperature above 15° C. (59° F.) is necessary, since a greater quantity of the salt will have been dissolved. In the official test the residue left upon drying the mixture of quinine, ammonium sulphate, and water consists chiefly of quinine sulphate, thus; $2C_{20}H_{24}N_2O_2+(NH_4)_2SO_4=(C_{20}H_{24}N_2O_2)_2H_2SO_4+2NH_3$.

QUININE BISULPHATE. $C_{20}H_{24}N_2O_2H_2SO_4+7H_2O$. When neutral quinine sulphate is dissolved in water with the calculated necessary quantity of sulphuric acid an acid salt will be formed, which can be obtained of the above composition by crystallization. Its solution in water shows a strong blue fluorescence and has a strong acid reaction. The salt contains a larger proportion of water of crystillization, 23 per cent., than other quinine salts, which it loses if heated to the temperature of boiling water.

QUININE HYDROBROMIDE. $C_{20}H_{24}N_2O_2HBr+H_2O$. This salt, also known in commerce as quinine bromide, can be made by dissolving the alkaloid quinine in warm diluted hydrobromic acid until neutralized and crystallizing the solution. It has also been obtained by double decomposition between an aqueous solution of potassium bromide and a warm alcoholic solution of quinine sulphate, the resulting potassium sulphate being precipitated, while the quinine hydrobromide is subsequently recovered by crystallization from a concentrated solution.

Quinine hydrobromide has been largely used for hypodermic medication.

QUININE HYDROCHLORIDE. $C_{20}H_{24}N_2O_2HCl+{}_2H_2O$. Like the preceding salt, quinine hydrochloride can also be made by double decomposition, but is usually obtained by dissolving the alkaloid quinine in sufficient diluted hydrochloric acid to form a neutral solution and allowing this to crystallize. This salt differs from other quinine salts in being the most soluble in water and in the absence of the usual blue fluorescence from concentrated solutions unless acidulated with sulphuric acid; an excess of hydrochloric acid does not affect it. It is commonly called muriate of quinine by dealers.

QUININE SULPHATE. $(C_{20}H_{24}N_2O_2)_2H_2SO_4 + 7H_2O$. The official salt is the neutral sulphate, although termed by some basic sulphate; it is also known as quinine disulphate, but this term is incorrect and should not be used, diquinine sulphate indicating the true chemical composition. The manufacture of this most important alkaloidal salt has already been explained in connection with the preparation of quinine alkaloid. In order to insure a large yield of the salt it is necessary that the hot solution from which it is to crystallize be of a neutral reaction; the sulphates of the other alkaloids present are all far more soluble in cold water than quinine sulphate, and will, therefore, almost wholly remain in the mother-liquors. Small quantities of the lesser alkaloids are no doubt always present in the commercial article, but should not be detectable by the official test with ammonia water; the United States Pharmacopœia fixes no percentage limit of impurities, which in the British Pharmacopœia is placed at 5 per cent.

The official test with ammonia water, known as Kerner's test, depends upon the greater solubility of the sulphates of the other cinchona alkaloids in cold water and the greater solubility of quinine alkaloid in ammonia water. DeVrij and Schaefer have shown that as much as 10 or 12 per cent. of lesser cinchona alkaloids may escape detection by Kerner's test, hence the German Pharmacopœia has adopted a modification by Kerner and Weller, which consists in digesting in a test tube 2 Gm. of quinine sulphate dried at 40° or 50° C. (104° or 122° F.) with 20 Cc. of distilled water at 60° or 65° C. (140° or 149° F.) for 30 minutes, with frequent agitation. The tube and contents are then cooled and kept at a temperature of 15° C. (59° F.) for two hours, with frequent agitation, after which the mixture is filtered; 5 Cc. of the filtrate should yield a clear solution with 4 Cc. of 10 per cent. ammonia water. This test is much more severe than that of the United States Pharmacopœia, and demands a much purer salt. Whenever solutions of alkaloidal salts are filtered it should be borne in mind that filter paper abstracts appreciable quantities of the salt from solution; it should, therefore, either be filtered through glass wool or the filtrate through paper should be

collected in fractions of 5 Cc. each., of which the second or third fraction only should be used for the above test.

Chemically pure quinine sulphate has been offered for sale for some time. This is obtained by first preparing pure quinine bisulphate by repeated recrystallization, and then exactly neutralizing a hot aqueous solution thereof with sodium carbonate, when, upon cooling, pure quinine sulphate will crystallize out.

The most convenient test for chemically pure quinine sulphate is either Schaefer's test with potassium oxalate or DeVrij's test with potassium chromate; both depend upon the very sparing solubility of the respective quinine salts. Schaefer's test is made as follows: 1 Gm. of official or 0.85 Gm. of anhydrous quinine sulphate is dissolved in 35 Cc. of distilled water by means of heat in a small flask previously tared; a solution of 0.3 Gm. of crystallized neutral potassium oxalate in 5 Cc. of water is then added, the contents of the flask made to weigh 41.3 Gm. by addition of distilled water, and the mixture kept at a temperature of 20° C. (68° F.) for thirty minutes, with occasional agitation.

After filtration one drop of solution of soda added to 10 Cc. of the filtrate should produce no turbidity within 3 or 5 minutes. Less than 1 per cent. of other cinchona alkaloids can be detected by this method.

Quinine sulphate can be crystallized with varying proportions of water, the official salt being allowed as much as 16.18 per cent. As the salt effloresces upon exposure, the symbolic formula given in the Pharmacopœia representing 14.43 + per cent. of water probably indicates the average composition of the commercial salt. Very appreciable loss of weight has been observed in cases where the salt was preserved in simple paper boxes, hence manufacturers now use either glass or tightly sealed tin containers.

The emerald-green color mentioned in the Pharmacopœia as occurring when a dilute aqueous solution of the quinine sulphate is mixed with a little bromine water and an excess of ammonia water is due to the formation of a resinous body to which the name *thalleioquin* (from the Greek word *θάλλός*, a green branch) has been given. Chlorine water may be used in place of bromine water, but, according to Flückiger, the latter is more sensitive, detecting as little as 1 part of quinine in 20,000 of solution. The thalleioquin reaction is characteristic of quinine salts, but is also obtained with quinidine.

QUININE VALERIANATE. $C_{20}H_{24}N_2O_2.HC_5H_9O_2 + H_2O$. This salt may be conveniently prepared by dissolving freshly precipitated quinine alkaloid in warm water by means of valerianic acid and crystallizing the solution upon cooling. It is decomposed at the temperature of boiling water, losing valerianic acid.

SPARTEINE SULPHATE. $C_{15}H_{26}N_2H_2SO_4 + 4H_2O$. Sparteine is the only alkaloid belonging to the class of amines recognized in the

Pharmacopœia. It is a liquid heavier than water and has been obtained by extracting scoparius with water acidulated with sulphuric acid, concentrating the infusion, decomposing the salt with sodium hydroxide and distilling. The distillate is supersaturated with hydrochloric acid, evaporated to dryness and distilled with the aid of potassa; first ammonia passes over, after which sparteine distils and condenses as a thick oily liquid. Another method consists in exhausting the powdered drug with 60 per cent. alcohol, evaporating the tincture at a low temperature and extracting the alkaloid with the aid of tartaric acid; the solution of sparteine tartrate is then decomposed with potassium carbonate, and the alkaloid thus liberated abstracted with ether. Pure sparteine is a colorless fluid, boiling at 287° C. (548.6° F.) and having an aniline-like odor and intensely bitter taste. It is easily decomposed upon exposure to air and light.

Sparteine sulphate is prepared by neutralizing the purified alkaloid with diluted sulphuric acid and rapidly concentrating the solution, when colorless crystals will be obtained. As indicated by the official formula it is the salt of a diacid base. The Pharmacopœia recognizes the presence of 4 molecules (17.8 per cent.) of water of crystallization, which represent about the average commercial products, as the amount of water varies from 3 to 5 per cent.

STRYCHNINE. $C_{21}H_{22}N_2O_2$. This alkaloid occurs in combination with igasuric acid, generally associated with brucine, in the Strychnos Nux vomica and other members of the natural order Loganiaceæ. The proportion of strychnine present in the seed varies, sometimes reaching as high as 1.8 per cent.

To extract the alkaloids the powdered drug may be exhausted with boiling water acidulated with hydrochloric or sulphuric acid, whereby the igasuric acid is liberated and the alkaloids obtained in solution as hydrochlorides or sulphates. Upon concentration of the infusion and addition of milk of lime the alkaloids are precipitated, and by collecting upon a strainer and washing the residue with water much foreign matter is removed. Subsequent treatment of the residue with cold diluted alcohol removes brucine, the treatment being continued as long as the washings are reddened by nitric acid, after which boiling alcohol is used to extract the strychnine; this, after recovery of the alcohol, is converted into sulphate by solution in diluted sulphuric acid, filtered through animal charcoal and precipitated with an alkali.

Some manufacturers exhaust the drug with hot alcohol of about 60 per cent., concentrate the tincture, filter and add lead acetate, whereby the igasuric acid is removed together with coloring-matters, while the alkaloids remain in solution as acetates. After a second filtration the alkaloids are precipitated by ammonia and may be further treated as above or dissolved in hot alcohol, from which the strychnine will crystallize on cooling, and may be freed from adhering brucine by washing with diluted alcohol.

Commercial strychnine occurs both in the form of crystals and powder, the latter being preferred for dispensing purposes. Its taste is so intensely bitter that it is perceptible if but $\frac{1}{8}$ grain be dissolved in 10 gallons of water.

The blue color obtained when strychnine is added to a solution of potassium dichromate and sulphuric acid is due to an oxidation-product, the exact nature of which is unknown, as it has not been possible to isolate the blue compound on account of its evanescent character.

STRYCHNINE SULPHATE. $(C_{21}H_{22}N_2O_2)_2H_2SO_4+5H_2O$. This salt is best prepared by dissolving the alkaloid strychnine in warm diluted sulphuric acid, avoiding an excess of the latter; if a hot saturated solution be obtained, the salt will crystallize with 5 molecules (about 10.5 per cent.) of water, as required by the Pharmacopœia. It represents about 78 per cent. of the alkaloid and is generally employed for solutions on account of its greater solubility.

VERATRINE. The substance recognized, both in the Pharmacopœia and commercially, by the name veratrine, is a mixture of alkaloids obtained from cevadilla seed. It consists of 3 crystallizable alkaloids, *cevadine*, $C_{32}H_{49}NO_9$; *sabadine*, $C_{29}H_{51}NO_8$, and *sabadinine*, $C_{27}H_{45}NO_8$; and 2 amorphous alkaloids, known as *veratrine*, $C_{37}H_{53}NO_{11}$, and *cevadilline* or *sabadilline*, $C_{34}H_{53}NO_9$; of these cevadine is the most important. Veratrine is not found in white or green hellebore, but other alkaloids, *jervine*, $C_{26}H_{37}NO_3$, and *veratroidine*, $C_{51}H_{78}N_2O_{16}$, have been isolated from these plants.

The mixture of alkaloids in cevadilla seed being very complex, no attempt is made at separation in the process of extraction, the crushed seed being exhausted with alcohol, which dissolves the alkaloids in their natural combination with veratric acid. The tincture is concentrated, mixed with water to remove fat and other impurities, and, after filtration, precipitated by ammonia in excess. The precipitate, having been washed with water, is dissolved in diluted hydrochloric or sulphuric acid, the solution decolorized with bone-black and the mixed alkaloids again precipitated by an alkali.

Owing to its intensely irritating effect upon the mucous membranes care is necessary in handling veratrine, and dampening with alcohol or expressed oil of almond will be found desirable when mixing it with other substances. Veratrine is rarely used internally, but mostly as oleate or ointment.

Besides the foregoing there are a number of alkaloids and alkaloidal salts not recognized in the Pharmacopœia, which are of more or less interest to pharmacists, and will, therefore, be briefly considered.

ACONITINE. $C_{34}H_{47}NO_{11}$. This alkaloid is the active principle of aconite root, in which it exists combined with aconitic acid. It

is usually extracted by means of alcohol acidulated with tartaric acid, and, after dilution of the tincture with water, removal of fat, resin, etc., by suitable methods, the alkaloid is precipitated by addition of sodium bicarbonate and dissolved in ether, from which it crystallizes. The investigations of Freund and Dunstan have recently thrown much light on the constitution of this alkaloid, which occurs in the drug to the extent of 0.2 or 0.3 per cent. Commercial aconitine is very rarely pure, being accompanied by aconine and other products, no doubt because it is easily split up by the action of heat and alkalies; six samples recently examined contained from 61.1 to 87 per cent. of pure alkaloid. Aconitine, when pure, should be completely soluble in ether, and to prepare it on a small scale aconitine nitrate may be dissolved in water, decomposed with sodium bicarbonate and shaken out with ether, from which it will crystallize upon spontaneous evaporation of the solvent. It melts at 197° C. (386.6° F.).

BERBERINE. $C_{20}H_{17}NO_4$. The chief interest attached to this alkaloid arises from the fact that, while the alkaloid is soluble in water, its salts are difficultly soluble, and are deposited in a crystalline form from acid liquids. Berberine occurs in several plants—in hydrastis to the extent of 3 or 4 per cent.—from which it may be obtained by adding to a concentrated aqueous infusion of the drug hydrochloric or sulphuric acid in excess, when the corresponding berberine salt will be deposited in crystals, which, after purification by recrystallization from boiling water, may be decomposed by means of freshly prepared lead hydroxide. After filtration and concentration of the filtrate, berberine will separate as a yellow crystalline powder.

CINCHONIDINE SALICYLATE. $C_{19}H_{22}N_2O.HC_7H_5O_3$. This salt, which has been used extensively by physicians, may be prepared by direct union of the alkaloid and acid. A neutral solution should be made in hot water or diluted alcohol and allowed to crystallize upon cooling; the salt is sparingly soluble in cold water.

CONIINE. $C_8H_{17}N$. Conium owes its medicinal virtues entirely to the volatile alkaloid, which is present in the unripe fruit (probably combined with malic acid), to the extent of 0.5 or 0.8 per cent. It can be extracted by exhausting the drug with water acidulated with acetic acid, evaporating the infusion down to an extract, in a vacuum apparatus, adding an alkali carbonate and distilling. By collecting the distillate in diluted sulphuric acid, coniine sulphate is at once formed, which may be freed from the accompanying ammonium salt by treatment with alcohol and ether, in which the latter is insoluble; by addition of an alkali to the alcohol and ether solution and distillation, coniine will be isolated, and may be dissolved in ether, from which it can be obtained as hydrochloride, by passing

dry hydrochloric acid gas into the solution, the salt being insoluble in ether. Coniine hydrochloride occurs in white crystals, which are non-deliquescent, may be dried at 100° C. (212° F.) without decomposition, and are soluble in water and alcohol.

Coniine belongs to the amines, and has been prepared synthetically by Ladenburg; it has a strong alkaline reaction and a penetrating, suffocating odor. When pure it is a colorless, oily liquid, lighter than water, and boiling at 169° C. (336.2° F.).

CORNUTINE. This alkaloid, having been but recently isolated, has not yet been sufficiently studied to give a full account of its composition, properties, etc. According to Keller and others, both the parturient and hæmostatic effects of ergot reside in this basic principle, which appears to be present in varying quantities in the different commercial varieties of ergot. It is soluble in ether, and has been obtained in long, colorless, needle-shaped crystals. Keller claims that picrosclerotine, ergotinine, and the cornutine extracted by him are identical, the former two representing impure forms of the latter. As characteristic reactions of the alkaloid, he mentions the following two: 1. If a solution of cornutine in concentrated sulphuric acid be allowed to stand for several hours, it will assume a violet-blue color. 2. If a drop of ferric chloride solution be added to a solution of the alkaloid in sulphuric acid, an intense orange-red color is produced, which, upon standing, gradually changes to bluish-green and finally to violet.

HYDRASTINE. $C_{21}H_{21}NO_6$. This body must not be confounded with the mixture of resinoid substances sold under a similar name, hydrastin. The alkaloid, hydrastine, occurs in the root of hydrastis canadensis, golden seal, associated with berberine, and in commerce is frequently designated as the white alkaloid of hydrastis. Exactly how hydrastine exists in the drug was, for a long time, uncertain, some authorities contending that it is combined with an acid, and others that it exists free. According to recent investigations (September, 1895) by Dohme and Engelhardt, a portion of the alkaloid, about 20 per cent. of the total yield, exists in a free state, the remainder being in combination with an acid, the nature of which has not yet been determined. While formerly supposed to be present only in small proportions, hydrastine has now been shown to occur to the extent of 2.33 per cent. in the fresh or 3.14 per cent. in the dried root.

In extracting hydrastine for commercial purposes, it becomes necessary first to remove the berberine, as stated under that alkaloid; the residuary liquors, after concentration and dilution with water to remove resins, fat, etc., are precipitated with ammonia in excess, whereby crude hydrastine is separated, which may be purified by resolution in diluted sulphuric acid, reprecipitation by means of ammonia, and repeated crystallization from hot alcohol.

Hydrastine is a weak base melting at 135° C. (275° F.), which, while readily soluble in acidulated water, forms difficultly crystallizable salts. It is extensively used in preparing the so-called "colorless hydrastis," which is a solution of the alkaloid in a mixture of water and glycerin with the aid of hydrochloric or sulphuric acid.

MORPHINE MECONATE. $(C_{17}H_{19}NO_3)_3H_3C_7HO_7$. This salt is not used in medicine, but, under the name "Solution of Bimeconate of Morphine," the British Pharmacopœia recognizes a preparation made by precipitating a solution of nine grains of morphine hydrochloride with ammonia water, and, after washing the resulting precipitate of morphine, dissolving it in a mixture of one-half fluidounce of alcohol and one and one-half fluidouces of distilled water with the aid of six grains of meconic acid.

NARCOTINE. $C_{22}H_{23}NO_7$. This substance occurs in opium, sometimes to the extent of 10 per cent. and over. Being readily soluble in chloroform and ether, it is easily extracted from powdered opium by maceration or percolation with either of these solvents, and is, therefore, not found in two official preparations of the drug, namely, deodorized opium and tincture of deodorized opium. Narcotine is a very weak base and does not neutralize acids; it exists in opium in a free state, and, although it forms crystallizable compounds with hydrochloric and sulphuric acids, these are readily decomposed by an excess of water, and yield narcotine to both ether and chloroform when shaken with these liquids. A solution of narcotine in sulphuric acid soon becomes yellow, and, upon heating, turns red and finally purple.

PILOCARPINE NITRATE. $C_{11}H_{16}N_2O_2.HNO_3$. This salt, which is preferred by some to the hydrochloride, may be obtained by neutralizing a solution of pilocarpine with nitric acid and crystallizing. It is recognized in the British Pharmacopœia.

QUININE SALICYLATE. $C_{20}H_{24}N_2O_2.HC_7H_5O_3$. This salt may be prepared by neutralizing an alcoholic solution of quinine with salicylic acid and allowing the solution, after concentration, to crystallize; it can also be obtained, as a curdy precipitate, by mutual decomposition between solutions of quinine hydrochloride and ammonium salicylate, which can be dissolved in alcohol and crystallized in an anhydrous state.

QUININE TANNATE. $C_{20}H_{24}N_2O_2(C_{14}H_{10}O_9)_2$. Although tannic acid is known to precipitate quinine from a neutral solution of its salts in water, this compound is intentionally used by physicians on account of its very sparing solubility, which renders its bitter taste less perceptible. The salt is usually prepared by adding a solution

of 1.8 parts of tannic acid in 18 parts of water to a solution of 1 part of quinine sulphate in 30 parts of water, made with just sufficient sulphuric or preferably acetic acid. Any excess of acid is carefully neutralized with ammonia and the precipitate allowed to subside, then washed on a filter with water, being afterward dried at a very moderate heat. Quinine tannate is officially recognized in the German Pharmacopœia.

CHAPTER LX.

NEUTRAL PRINCIPLES AND GLUCOSIDES.

BESIDES organic acids and alkaloids, plants furnish a number of valuable principles which have a neutral reaction, and, for convenience, are divided into bitter principles and glucosides, the former being also known as amaroids. The distinguishing feature of the latter class is, that when treated with diluted acids or ferments they split up into glucose, and a new body, differing from the original article acted upon, but characteristic of that substance. With very few exceptions, glucosides do not contain nitrogen. Although glucosides are an important group of plant-products, only one is officially recognized in the Pharmacopœia, partly due to the fact that they do not always constitute the active principle of the plant, and are in many cases associated with other bodies. A few glucosides appear to have a dual character, for, while yielding glucose by the treatment above mentioned, some also possess basic and others acid properties. As stated in the previous chapter, both glucosides and bitter principles are distinguished from alkaloids by the ending *in* or *inum*.

The following official neutral principles are used by physicians to a greater or less extent: aloin, chrysarobin, elaterin, glycyrrhizin, picrotoxin, salicin, and santonin; of these, salicin is a true glucoside.

ALOIN. The name aloin is used, both commercially and in the Pharmacopœia, to designate the neutral, crystalline principle upon which the activity of aloes depends, irrespective of the source, although the Pharmacopœia does specify two varieties, namely, that derived from Barbadoes and Socotra aloes. The names *barbaloin*, *socaloin*, and *nataloin* are used to designate the aloins obtained from different sources, which may also be distinguished by special tests. It is probable that barbaloin constitutes the bulk of the commercial aloin. Cape aloes has thus far not yielded any crystallizable substance, but a yellow flocculent precipitate may be obtained by addition of bromine to an aqueous infusion.

Aloin, being wholly soluble in water, is usually obtained by treating aloes with hot water, to which a little hydrochloric or sulphuric acid has been added; after the infusion has been allowed to stand for a day, it is carefully decanted from sediment, concentrated at a moderate temperature and set aside, when crystals or crystalline crusts of aloin will separate. The aloin may then be purified by recrystallization from hot water or very dilute alcohol. The addition of a little acid has been found advantageous in avoiding the contamination

of aloin with non-crystallizable matter, which is less soluble in acidulated water than in plain water.

This process is well adapted for the manufacture of barbaloin, but for socaloin the powdered drug is preferably mixed with a little diluted alcohol and strongly expressed, after which the residue (press-cake) is dissolved in warm, weak alcohol, and the solution allowed to crystallize. Nataloin differs from the other two in being sparingly soluble in cold and hot water, and must be extracted by treatment with hot alcohol, after the drug has previously been treated with water; it can be recrystallized from methyl alcohol, in which it is readily soluble. It is rarely found on the market.

Aloin of commerce is often contaminated with resinous and other matter, which can be detected by imperfect solubility of the sample in cold water. As stated in the Pharmacopœia barbaloin differs from socaloin in yielding with cold nitric acid a crimson color; heat must not be used in this test, as socaloin, when heated with nitric acid, gives similar results.

CHRYSAROBIN. This principle, derived from Goa Powder by treatment with hot benzene, is frequently confounded in commerce with chrysophanic acid. As thus obtained it is still contaminated with some impurities, but corresponds to the requirements of the Pharmacopœia; it can be obtained pure, in the form of small yellow scales, by repeated crystallization from acetic acid, and then has the composition $C_{30}H_{26}O_7$. By oxidation chrysarobin is gradually converted into *chrysophanic acid*, $C_{15}H_{10}O_4$, which latter substance forms deep-red solutions with the alkalies; the change of color mentioned in the Pharmacopœia as occurring when chrysarobin dissolved in potassa solution is exposed in a test-tube is due to the formation of this acid by absorption of oxygen from the air.

ELATERIN. $C_{20}H_{28}O_5$. Commercial elaterium owes its medicinal virtues to a neutral principle called elaterin, which may be extracted by treatment with chloroform and subsequent addition of ether to the chloroformic solution, whereby crystals of elaterin are precipitated, being practically insoluble in ether. The crystals may be further purified by washing them with a little ether and recrystallizing from chloroform. The yield of elaterin varies from 25 to 35 per cent. of the weight of elaterium, and the two substances must not be confounded with each other.

GLYCYRRHIZIN. This substance, although for a long time considered to be a neutral principle and also a glucoside, is now looked upon as a tribasic acid, *glycyrrhizic acid*, having the composition $C_{44}H_{63}NO_{18}$, which exists in liquorice root in combination with ammonia as an acid salt. It possesses no medicinal properties, and is valuable only on account of its very sweet taste. It is recognized in the Pharmacopœia in combination with ammonia as *ammoniated gly-*

cyrrhizin, and, in the official process for the preparation of this compound, the complete extraction of glycyrrhizin from the drug is insured by adding ammonia water to the menstruum, so that a neutral ammonium glycyrrhizate may be formed. The addition of sulphuric acid to the percolate causes the precipitation of the glycyrrhizin, which, for the purpose of purification, is collected, redissolved in ammonia water, and again precipitated, being finally dissolved in sufficient ammonia water and obtained in scales by spreading the solution on glass and drying. When boiled with diluted sulphuric acid pure glycyrrhizin splits up into glycyrrhetin, $C_{32}H_{47}NO_4$, and parasaccharic acid, $C_6H_{10}O_8$, which latter reduces Fehling's solution like glucose and thus gave rise to the former view that glycyrrhizin was a glucoside.

PICROTOXIN. $C_{30}H_{34}O_{13}$. The neutral principle present in cocculus can be obtained by exhausting the bruised seed with hot alcohol, concentrating the tincture to a thick syrupy consistence, removing separated fat and boiling the residue with water. After filtration of the decoction picrotoxin will crystallize upon cooling of the filtrate, and may be purified by recrystallization from alcohol.

SALICIN. $C_{13}H_{18}O_7$. Several methods are in use for the extraction of this principle from willow and other barks. The bark may be macerated and boiled with milk of lime, the decoction, after straining, being allowed to subside; the clear liquid is concentrated, treated with animal charcoal and evaporated to dryness, after which the residue is exhausted with weak alcohol, from which the salicin will crystallize after removal of the alcohol by distillation. Another plan is to exhaust the bark with boiling water and deprive the decoction of coloring matter and tannin by digestion with litharge or treatment with basic lead acetate; any free acid present in the liquid is neutralized with chalk. The filtrate, on concentration, will yield crystals of salicin, which may be purified by recrystallization.

Salicin is the only true glucoside officially recognized. When boiled with diluted sulphuric acid it takes up water and splits up into glucose and saligenin or salicyl alcohol, thus, $C_{13}H_{18}O_7+H_2O=C_6H_{12}O_6+C_7H_8O_2$.

A characteristic reaction of salicin is the production of a bright red color when the substance is dissolved in concentrated sulphuric acid, followed by the separation of a dark-red powder upon addition of water, the solution becoming colorless. The production of the fragrant odor of the oil of meadow sweet when salicin is heated with diluted sulphuric acid and potassium dichromate also serves to distinguish this substance from others; the odor is due to the formation of salicyl aldehyde.

SANTONIN. $C_{15}H_{18}O_3$. Chemically santonin is the anhydride of a weak acid, although generally looked upon as a neutral substance.

It is obtained by mixing ground wormseed with slaked lime and exhausting the mixture with hot water; the resulting solution of calcium santoninate is concentrated and decomposed with hydrochloric acid. The crude santonin is treated with diluted ammonia water, dissolved in alcohol, and the solution decolorized with bone-black, after which it is allowed to crystallize.

Santonin possesses the property of turning yellow when exposed to the light and then forms a yellow solution with alcohol, from which, however, it again crystallizes colorless.

The following may be mentioned as characteristic reactions of santonin: a bright pinkish-red color is produced when santonin is added to an alcoholic solution of potassa; if 0.010 Gm. of santonin be added to a mixture of 1 Cc. each of sulphuric acid and water a colorless solution is obtained, which, when heated, assumes a violet color upon addition of one drop of ferric chloride solution.

CHAPTER LXI.

ANIMAL FERMENTS.

AMONG the digestive agents found in the animal body, two have received recognition in the Pharmacopœia. It is well known that the digestion of food is of a twofold character; one takes place after the food has entered the stomach and is called gastric or peptic digestion, the other, occurring after the partly digested food leaves the stomach, is known as pancreatic or intestinal digestion. During the mastication of food it becomes mixed with the secretion of the salivary glands, which contains a substance known as *ptyalin*, belonging to the class of unorganized ferments usually termed enzymes by physiologists, from the Greek word *enzymos*, meaning fermented. The special action of ptyalin appears to be to prepare starchy food for subsequent digestion, as it is capable of converting starch into dextrose; in the presence of hydrochloric acid even as weak as 0.4 per cent., it is rendered inert, being most active in slightly alkaline liquids.

The action of ferments upon food depends upon the character of the latter, as the different ferments have specific functions and cannot be used indiscriminately for all kinds of food. Food partaken of by animals is either albuminoid or amylaceous in its nature, the former being converted into peptones, the latter into sugars. The digestive action of ferments on albuminoids is called the proteolytic action, from the word *proteolysis*, meaning the change occurring in proteids while being digested; the digestion of amylaceous food, on the other hand, is known as the amylolytic action of ferments, from *amylolysis*, meaning the conversion of starch into sugar.

The various products formed during the digestion of food are syntonin, albumoses, and peptones. The first, also known as acid albumin, is probably produced by the action of hydrochloric acid (of which gastric juice contains from 0.1 to 0.25 per cent.) on albuminoid substances, and occurs soon after the ingestion of food. After peptic digestion has set in albumoses are formed, which are gradually converted into peptones, the end-products of digestion and the form in which albuminoid food is assimilated, peptones being readily diffusible and absorbed by a process of dialysis. As stated before, digestion is not completed in the stomach; the mixture of albumoses and peptones, forming a smooth, pulpy mass called chyme, passes into the intestines, where the conversion into peptones and other diffusible products is completed.

Pancreatin and pepsin are the two agents secreted in the body of

all animals, without which assimilation of food would be impossible; both have been recognized in the Pharmacopœia and are largely used by physicians.

PANCREATIN. By this name is recognized a mixture of enzymes found in the pancreatic juice, the secretion of a gland deeply seated in the abdomen, known as the pancreas. The pancreatic juice is a clear, colorless, somewhat viscid liquid of an alkaline reaction, without odor and of an insipid, somewhat saline taste; it possesses both proteolytic and amylolytic activity, besides being capable of emulsifying fatty matter.

The Pharmacopœia gives no directions for the preparation of pancreatin and different manufacturers probably pursue different methods. The following was suggested in the first edition of the National Formulary: Fresh pancreas of the hog, freed as much as possible from fat and adhering membranes, is reduced to a fine paste by means of a suitable mincing-machine; it is next mixed with half its weight of cold water and kneaded thoroughly and frequently during one hour, after which the mass is transferred to a strainer and forcibly expressed; the liquid is filtered as quickly as possible through flannel, and to the filtrate is added an equal volume of alcohol; the precipitate is collected, drained, and freed by pressure from as much of the adherent liquid as possible; it is then spread on shallow trays, dried by exposure to warm air at a temperature not exceeding 40° C. (104° F.) and reduced to powder. When large quantities of pancreas are operated upon it is advisable to use water saturated with chloroform, which will retard decomposition for a long time.

In some instances the finely minced pancreas is macerated with highly diluted hydrochloric acid, in place of plain water, and the fat is often removed from the powdered mass by means of purified benzin.

There are supposed to be no less than four unorganized ferments present in the pancreatic juice—namely, *trypsin*, for the digestion of albuminoids; *amylopsin*, for carbohydrates; *steapsin*, for fats; and a rennet ferment, which coagulates milk. Trypsin has been isolated in a comparatively pure state; it differs from pepsin in several important particulars, acting best in an alkaline medium, and, although active in a neutral or even faintly acid solution, it is completely destroyed in acid liquids even as weak as gastric juice. Amylopsin very closely resembles diastase and ptyalin, both in action and properties, though in converting starch into maltose and dextroglucose it is much more energetic than ptyalin. Steapsin, or fat-digesting ferment, appears to exert a special action in the emulsification of fats and more particularly in the presence of the alkali salts of the biliary acids, thus preparing them for better absorption. The milk-curdling ferment is probably identical with that found in the stomach.

Pancreatin usually appears in the form of a yellowish, yellowish-white, or grayish-white powder, or in that of transparent, brittle, yellowish scales, which are odorless or have a faint, peculiar, not unpleasant odor, and a somewhat meat-like taste. It is slowly and almost completely soluble in water, but insoluble in alcohol.

Pancreatin digests albuminoids and converts starch into sugar, in presence of alkalies; prolonged contact with acids renders it inert. It is hygroscopic, and, when exposed to the air for some time, loses its value; hence it should be preserved in well-stoppered bottles. Dilution with sugar of milk seems to retard deterioration, saccharated pancreatin having been found to retain its peptonizing value far better than the pure article. The aqueous solution of pancreatin is a clear, pale-yellowish liquid, which is precipitated by heat, by alcohol, and by hydrochloric acid, but not by a saturated solution of sodium chloride.

Although the proteolytic value of commercial pancreatin is probably the most important (as shown by the Pharmacopœial test), yet its action on carbohydrates should likewise be observed. Some samples have been found to peptonize milk very readily, and yet exert little or no effect on starch-paste, and *vice versa*. For testing pancreatin a 5 per cent. starch mucilage is better suited than a stronger preparation, and the length of time required for the complete conversion of starch into sugar should be noted; usually, good pancreatin is supposed to convert six or eight times its weight of starch in a few minutes, the test being conducted at a temperature of 43.3°–46.1° C. (110°–115° F.). The fact that pancreatin liquefies starch-paste is not sufficient, as this may be due to the simple change of the starch into dextrin; a little of the liquid should be added to water every few minutes and tested by means of a drop or two of some very dilute iodine water; as soon as the purplish or pinkish color fails to appear, the conversion into sugar is complete. The less the time required for this change the better is the quality of the pancreatin.

Pepsin. This ferment was discovered in 1836, by Schwann, after Eberle had furnished proof that digestion of food in the stomach is due neither to the mechanical action of the mucous membranes nor to the solvent action of acids, but is dependent upon some unorganized ferment present in the gastric juice; this ferment was determined by Schwann and named pepsin, from the Greek word πέψις (digestion). Pepsin is a secretory product of certain glands imbedded in the tissue of the inner coating of the stomach, but has also been found in muscular tissue, urine, brain, and the mucous membrane of the intestines. True or active pepsin probably does not exist at all times in the gastric juice, but is formed by the action of hydrochloric acid and chlorides from a mother-substance known as *pepsinogen*, as the digestive functions of the stomach may require; in support of this theory it has been found that glycerin will abstract

increased quantities of pepsin from the mucous membrane of the stomach after this has been treated with 0.2 per cent. hydrochloric acid, or 1.0 per cent. sodium chloride solution. The use of pepsin in medicine is mainly due to the efforts of Dr. Corvisart, court physician to the Emperor Napoleon III., but the quality of the commercial article has been vastly improved since that time; to the perseverence and energy of American pharmacists are due the improvements in the mode of manufacturing pepsin and the wonderful increase in digestive power of the commercial article.

In this country two kinds of pepsin are manufactured, known respectively as precipitated pepsin and soluble or scale pepsin; the former is made by the method recommended by E. Scheffer, in 1872, which consists in precipitating an acid infusion (prepared cold) of clean mucous membrane of hog stomach by a saturated solution of sodium chloride, redissolving the precipitate in acid water, reprecipitating with salt in order to purify the pepsin, and finally drying at or below 40° C. (104° F.). A full account of this process may be found in the *American Journal of Pharmacy* for 1872. The process for the manufacture of the so-called scale or peptone pepsins insures an increased yield of product and higher digestive power, but not always the same degree of purity; it consists in subjecting the well-cleaned mucous membranes of animal stomachs, after being thoroughly minced by machinery, to a process of self-digestion in water acidified by hydrochloric acid at a temperature of 38°–45° C. (100.4°–113° F.), until the whole mass is converted into a uniform, transparent, glairy fluid. This is allowed to cool and deposit over night, after an addition of chloroform or sulphurous acid solution, which prevents putrefaction and in no wise interferes with the activity of the pepsin; the liquid is carefully strained, concentrated in a vacuum apparatus to a syrupy consistence, and spread upon plates of glass, where it is allowed to scale in suitable dust-free rooms. Pepsin thus prepared always contains mucus, peptones, and syntonin, while that prepared by the Scheffer method is contaminated with salt and some inert albuminous matter. In 1891 a process was patented in this country and in England, combining the advantages of the two preceding processes. The essential features are as follows: the well-cleansed and minced mucous membranes are brought to solution by digesting with acidulated water, the solution being clarified after the addition of sulphurous acid; the clear liquid is separated from the deposit and then precipitated by saturating, at a higher temperature, with sodium sulphate, whereby the pepsin is deposited while the peptone remains in solution. The precipitated pepsin is dissolved in weak hydrochloric acid and subjected to dialysis, which removes the sodium sulphate and remaining peptones, after which the residual solution is concentrated at a low temperature and dried on plates of glass. The sodium sulphate is not lost in the process but reclaimed from the peptone solution by recrystallization. While the U. S. Pharmacopœia recognizes only the pepsin obtained from hog stomachs, the

British Pharmacopœia admits pepsin from the stomachs of hogs, sheep, and calves, and gives the following directions for its preparation: The stomach of one of these animals recently killed, having been cut open and laid on a board with the inner surface upward, any adhering portions of food, dirt, or other impurity are to be removed and the exposed surface slightly washed with cold water; the cleansed mucous membrane is then to be scraped with a blunt knife or other suitable instrument, and the viscid pulp thus obtained is to be immediately spread over the surface of glass or glazed earthenware and quickly dried at a temperature not exceeding 100° F. The dried residue is to be reduced to powder and preserved in a stoppered bottle.

The official British pepsin is thus seen to consist in part of the dried secretion of the mucous membrane, which naturally contains substances liable to putrefy, and this, no doubt, accounts for the offensive odor noticed in some samples dispensed in this country. Such a pepsin also has a weak digestive power, and the British Pharmacopœia does not demand that official pepsin shall dissolve more than fifty times its weight of hard-boiled egg albumen in thirty minutes, at a temperature of 54.4° C. (130° F.).

French pepsin is chiefly obtained from sheep stomachs, and Boudault's preparation contains starch and sometimes lactic acid. The German Pharmacopœia does not prescribe the source of official pepsin nor the manner of its preparation; the stomachs of hogs and calves are, however, usually employed. Official German pepsin is required to dissolve 100 times its weight of hard-boiled egg albumen in one hour, at a temperature of 45° C. (113° F.).

Pepsin exposed on a watch-glass to the air, even in damp weather, should not become sticky in the course of a few hours, showing the absence of an undue amount of peptone. It should form, with distilled water, an almost clear solution, which is not rendered turbid by the addition of acetic acid, showing the absence of mucus. (Pepsin made by Scheffer's process never yields a perfectly clear solution with water owing to the presence of syntonin or acid albumin.) It should be free from any disagreeable or ammoniacal odor due to the presence of putrescible matter. A drop of tincture of iodine added to a solution of pepsin should not develop a blue or purplish-red color, showing the absence of starch and dextrin.

The greater the proportion of peptone present in pepsin the more rapidly does it absorb moisture from the air, and the greater the absence of mucus the less unpleasant will be the odor and the more perfectly clear will be the solution of pepsin in water, especially if the water be acidulated with acetic acid. Except in minute quantities, sodium chloride impairs the activity of pepsin; the same is true of alcohol. An aqueous solution of pepsin will decompose in a short time; after addition of hydrochloric acid it remains clear but gradually loses its effects on albumen. Glycerin, on the other hand, preserves its virtues. Tannin and the alkali carbonates and bicarbon-

ates inhibit the proteolytic action of pepsin. At a temperature of 63° C. (145.4° F.) the activity of pepsin is destroyed.

The mere solution of hard-boiled egg albumen by pepsin in an acid menstruum is by no means an indication of its true value, as this can also be effected, under certain conditions, by hydrochloric acid and water alone. Complete peptonization or conversion of albumen into peptone appears to be a more positive test, but since the exact determination of peptones in a solution is only possible in the hands of the physiological chemist, the different pharmacopœias have adopted a simpler method of valuation.

Saccharated pepsin, prepared by intimately mixing one part of pepsin with nine parts of sugar of milk, is a convenient form of administering small doses of pepsin to children.

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